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Section of Dermatology.

[*December* 19, 1929.]

Benign Sarcoid Lymphogranuloma of Schaumann.—H. W. BARBER, M.B.

A. G., female, aged 40. Husband died from pulmonary tuberculosis, April, 1929.

The present eruption began as a small purple patch on the left cheek two years ago, since when further lesions have appeared extensively. She has had psoriasis since 1914.

There is a widespread eruption of sarcoid lesions involving the face, trunk and limbs. These vary from large hypodermic nodules in various stages of resolution to small superficial lupoid nodules (e.g., on the left knee).

Two of the fingers show the swelling of the first phalanges with tapering of the distal ones (spina ventosa).

X-ray examination of the bones reveals several characteristic clear spaces in the metacarpals and phalanges.

A skiagram of the chest shows no sarcoid deposits, but there is evidence of calcareous changes in the bronchial glands.

Von Pirquet reaction completely negative.

A microscopic section shows characteristic tuberculoid infiltration.

? Leukæmide. Case for Diagnosis.—H. W. BARBER, M.B.

J. B., male, aged 50, market-salesman. Had a sore in 1916, which was diagnosed as syphilitic, and for which he was given a few injections of salvarsan. He was subsequently treated at the Lock Hospital with novarsenobillon, having about fifty injections in five years, and his Wassermann reaction was reported negative.

He has had the present eruption apparently for about two years, and according to his story, it has from time to time responded temporarily to novarsenobillon.

It is situated chiefly on the face, neck and trunk. On the face and neck are diffuse erythematous patches with a certain amount of induration. Here and there are definite nodules, similar to those on the body. These are seen chiefly over the back, chest and abdomen; some are very superficial, others deeper, and their colour varies from pinkish to bluish; all are definitely indurated. Wassermann reaction negative.

Leucocyte Count: Total: 8,100 per c.c. Differential: Polymorphonuclears 60·5%, eosinophils 2·5%, lymphocytes 25·5%, hyalines 10·0%, basophils 1·0%.

In spite of the negative blood-findings, I am inclined to regard this as a case of leukæmia of the skin, in which the characteristic changes in the leucocyte count have not yet appeared. Some years ago a case, with typical leukæmic nodules in the skin and enlarged glands, was observed by Dr. Dowling and myself, and the characteristic blood-changes were not found until shortly before death.

Sections: Microscopically there are seen dense masses of lymphocytes situated chiefly round the deeper vessels of the dermis.

The patient has had five injections of solganal and the nodules are now much reduced in size. Patches resembling lupus erythematosus have disappeared from his face.

? Lupus Erythematosus. Case for Diagnosis.—G. B. DOWLING, M.D.

Patient, male, aged 73. Seen at St. John's Hospital a month ago, complaining of an eruption on the left side of the face, which began three years ago on the temple and gradually spread by the formation of bullæ. These have occurred always at the periphery of the lesion, the central parts being marked by superficial atrophy. He states that the blisters have sometimes been as large as walnuts, but generally of about the size of a pea. The eruption has always been accompanied by intense irritation.

When I first saw him he had very much the same condition as may be seen now, a fairly large scarred area, occupying most of the left side of the face, and extending up into the scalp slightly beyond the hair margin, with some excoriated superficial erosions and a number of fresh peripheral bullæ. To-day there are only one or two small bullæ about the periphery of the area. He states that he has never been without one or two blisters, either coming up or subsiding, and not more than a few days have elapsed without fresh ones. It has therefore been a very slowly progressive lesion, though it has apparently remained about the same size during the past year. I suggested to his medical attendant that the diagnosis might be lupus erythematosus, but I stated that I had never seen a case of the fixed type of this disease accompanied by bullæ. I advised a course of krysolgan injections.

Discussion.—Dr. A. M. H. GRAY said this was a case of great interest. He could not agree with Dr. Dowling that it was one of lupus erythematosus. He did not think that bullæ could develop except in acute lesions; the only bullæ that had been described were associated with intensely œdematous lesions, and they might be either clear or contain blood; often they were full of blood. He could not conceive how they could occur in a chronic fixed type of lesion. In this case there was not any of the hyperkeratosis so characteristic of lupus erythematosus. He did not know, however, what was the condition in this case.

There was an interesting group of bullous lesions which were associated with scarring. Some years ago he had shown before the Section an old man who had extensive lupus, not of an active type but slowly-spreading and non-ulcerative. That bullæ had developed chiefly on the legs, and their clearing-up always left scars. He brought the case with the suggested diagnosis of bullous tuberculide. All members must have seen cases of bullæ developing without apparent cause. These bullæ were, as a rule, sterile on culture, but they cleared up with scarring. It would be worth while to investigate the nature of the granuloma histologically.

The PRESIDENT agreed with Dr. Gray that some bullous eruptions were extraordinarily obscure and difficult to diagnose. Dr. Barron and himself had a case, in the Westminster Hospital, of a man with a patch resembling impetigo on his face, which failed to clear up under ordinary treatment, and typical pemphigus had now developed all over the body. He had under his care another case in which large bullæ had developed on the scalp causing cicatricial baldness. Bullæ were also present in the mouth. This condition had been going on for several months, during which no lesions had occurred elsewhere.

Dr. H. T. BARRON said that the original patch in the case referred to by the President appeared at the beginning of January, 1929, after a febrile illness said to be influenza. The lesion measured 3½ in. by 3 in., was more or less circular, and was on the upper part of the forehead and a portion of the scalp. It was strictly circumscribed, not gradually fading into healthy skin. When he first saw the case there was a soft, thick, easily detached crust. The patient said that the patch had scarcely varied in size since the end of January—i.e., for eleven months—and that it took from three to four weeks to attain that size, and then remained stationary. Crusts re-formed almost as soon as they were removed. No further patch developed until a month ago, when a small lesion appeared on the back of the head (the patient was bald), and that lesion resembled almost exactly an ordinary small patch of impetigo contagiosa. A fortnight ago bullæ began to appear on the thighs, and the patient was now covered from head to foot with pemphigus vulgaris.

Lichen Planus of Zoster Distribution.—W. KNOWSLEY SIBLEY, M.D.

This is a zoniform lichen planus of two or three of the lower right ribs in a man aged 40, who was sent to the hospital a week ago as a case of herpes zoster. The rash had lasted three months and it was definitely zoniform, extending from the median line in front almost to the median line at the back. He also had lichen planus on the buccal mucosa. He has now a large number of lichen planus papules over many regions of the body. It is the most characteristic case of the kind I have seen.

Psoriasis and Syphilis, with Arsenical Pigmentation.—W. KNOWSLEY SIBLEY, M.D.

This patient is aged 26, and I showed him to a meeting of the Section in January, 1929. He had had psoriasis intermittently for five years. When exhibited in January he was deeply pigmented over the whole of the body and the pigmentation has remained ever since. At that time, too, he had considerable psoriasis. Yet, he said that twelve months previously his skin had been normal in colour. He had some palmar keratosis. There was an ulcer on the left ankle and palpable supra-trochlear glands; there were also some superficial lesions in the mouth. He had been taking arsenic for a year. The Wassermann and Sigma reactions were negative and have been so on repeated occasions. To-day, however, the reports are "strongly positive." Otherwise there has been no change. All the tests were carried out in the same laboratory. The psoriasis has gradually diminished. In January last I suggested a diagnosis of syphilis in addition to that of psoriasis. He has been having potassium iodide and mercury for some time.

? Psoriasis. ? Pityriasis Rubra Pilaris. Case for Diagnosis.—J. H. T. DAVIES, M.B.

This patient, a man aged 55, has had the present eruption for about ten years. He says that it began on the elbows and spread down towards the hands, and later appeared on the knees, extending towards the feet. Before coming under treatment, the eruption itched intensely, and the patient had trouble with cracking of skin on the back of the hands which was considerably thickened. The eruption has responded fairly well to an ointment of ammoniated mercury salicylic acid and tar.

It affects the extensor surfaces of the limbs symmetrically, and there are a few isolated patches on the trunk. The patches have a sharp outline and consist of an aggregation of scaly follicular papules. The patient has been under my observation intermittently for six months, and at no time has the aspect of the eruption varied.

On vitropressure, distinct nodules of cell infiltration can be demonstrated around the follicles on those portions of the skin from which the scales have been adequately removed by treatment. Microscopically, the lesions resemble those in psoriasis more than anything else. I had labelled the case tentatively as one of pityriasis rubra pilaris, but I think the general opinion is that the condition is psoriasis.

? Parapsoriasis: Case for Diagnosis.—J. H. T. DAVIES, M.B.

The patient is a woman, aged 35, whose rash appeared immediately after an operation for prolapse of the uterus four months ago. She says that it began in the inguinal and vulvar region, and that the patches, having once appeared, remain and itch intensely.

On the trunk, and especially about the axillæ and groins, are oval and round macules of a light brownish-pink colour. On the upper part of the chest and neck the lesions are confluent. They are not scaly. The edge is marked by slight rounded elevation, slightly paler in colour than the rest of the lesion, and the infiltration, seen to be investing the capillary network in the section, is visible to the naked eye as a faint marbling of the surface.

The Wassermann reaction is negative, and in other respects the patient is perfectly well.

Epidermolysis Bullosa in a Mother and Two Children.—S. E. DORE, M.D.

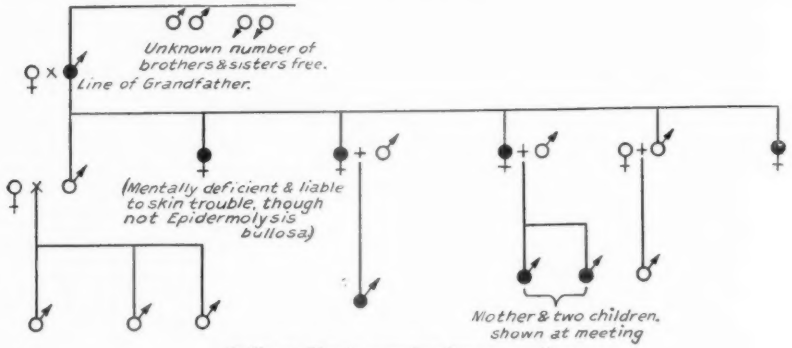
These cases have been shown here before. They were originally seen by Dr. Payne, then by the late Dr. W. F. R. Castle, who first showed the mother and the elder child at a meeting of this Section in 1922,[1] and then showed them again

[1] *Proceedings*, 1922, xvi (Sect. Derm., 53).

with the second child, born later, at a meeting in 1924.[2] Dr. Donald Paterson also showed them before the Section for the Study of Disease in Children.[3] There is nothing very unusual as regards the lesions, which mainly affect the neighbourhood of the joints, especially of the fingers and knees; the heels and the finger- and toe-nails are also involved. The bullæ appear after slight injury, and are sanguinous but not markedly hæmorrhagic. Various investigations have been carried out, but nothing strikingly abnormal was found.

An interesting feature concerns the genealogical tree (see chart). Apparently the first known occurrence of this condition was in the grandfather, who had six children (two males, four females). The two males married and had children, but these children were not affected. Of the four females, one was mentally deficient and is said to have been liable to various skin troubles, but not epidermolysis bullosa. Of the three other females who were affected two were married; one of these sisters had an only child (male) who was affected, the other sister had two male children affected; these are the two now shown. It seems that in this case the epidermolysis bullosa was transmitted through the female to the male, which is apparently unusual.

I think there may be cases of slight epidermolysis bullosa in which the condition is not recognized. I saw, not long ago, a child with a marked family history of bullæ occurring only on the feet; and I think Dr. Knowsley Sibley had a mild case in which there were only limited lesions.


Unknown number of brothers & sisters free.
Line of Grandfather.
(Mentally deficient & liable to skin trouble, though not Epidermolysis bullosa)
Mother & two children shown at meeting

Pedigree Chart; covering four generations.

Discussion.—Dr. KNOWSLEY SIBLEY said that the case of his, mentioned by Dr. Dore, was published in the *British Journal of Dermatology* in 1914, under the title of "A Recurrent Bullous Eruption" (with photograph). The patient, a woman, aged 63, gave no history of any earlier manifestation, except that she had always bruised easily. There was no other case in the family. She had had a recurrent bullous eruption on the front of both legs for thirty years, and on the posterior surface of the left forearm for ten years. There was not any affection of her nails. The lesions on the legs followed a blow from the tail of a large dog. At the time it bled a good deal, and a large blister appeared. The blebs had persisted in this region on and off ever since; often they broke and bled freely. There was always a considerable amount of irritation present before the blebs appeared.

Dr. A. M. H. GRAY said he had seen the whole family to which the President referred; they came to him originally. He believed that the sister of this woman was still alive. He had had two cases with bullæ on the feet, and these had been noted by Dr. Goldsmith in an article on bullous ichthyosis. He doubted whether those cases had anything to do with epidermolysis bullosa. The patients were only affected in the summer, and both had hyperhidrosis of the feet.

2 *Id.*, 1924, xviii (Sect. Derm., 25).
3 *Id.*, 1928, xxi, 1727 (Sect Dis. in Child., 89).

Erythema Multiforme.—S. E. DORE, M.D.

Patient, a boy, aged 3 years. The condition in this child is probably erythema multiforme bullosum. He has for two years suffered from an eruption of erythematous polycyclical figures all over the body, associated with the presence of bullæ, not only on the erythematous areas, but also on the normal skin. Apparently there is no itching, except when the bullæ first appear. The mucous membranes of the lips and nose have been affected and there has been a good deal of epistaxis from time to time.

I have had the case investigated in hospital, but nothing has been found to account for the eruption. There is no obvious toxic focus, and the tonsils and several diseased teeth have been removed without influencing the disease, and no treatment, with the possible exception of arsenic, has had any beneficial effect.

In such cases as this it is difficult to distinguish between pemphigus and dermatitis herpetiformis and bullous forms of erythema multiforme. There are some points in the present case in favour of dermatitis herpetiformis, but the comparative absence of itching and the marked circinate erythema seem to point to a diagnosis of a bullous erythema multiforme.

Discussion.—Dr. A. M. H. GRAY said that he took the opposite view, namely, that the condition was dermatitis herpetiformis of an unusual kind, largely for the reason that it was so persistent, and because the child had intense itching when the blisters were up. Dermatitis herpetiformis might be very anomalous in children; there were curious cases in which recurrent bullæ developed on the face and extremities. He had seen about five such cases. In one of them the eruption was generalized, and at one time was extraordinarily like typical dermatitis herpetiformis. He had never before seen a case like the present one.

The PRESIDENT (in reply) said that he had seen such cases as Dr. Gray had mentioned, but in those the presence of bullæ was the outstanding feature, whereas in this case the circinate erythema was more prominent.

Lichen Plano-pilaris.—H. MACCORMAC, C.B.E., M.D.

The patient, a woman, aged 67, a retired hospital nurse, first noticed the eruption $2\frac{1}{2}$ months ago on the back. From this time the rash has gradually spread further, and it is now present in grouped areas over the interscapular and presternal regions, the lumbar area, the buttocks, and the left antecubital fossa. There is also a papular rash on the lower lip, on the gums, and on the vulva. Itching is a pronounced feature, sufficient in degree to interfere with sleep.

The individual lesions consist of discrete small papules of a yellowish red colour, imparting a sensation of roughness to the finger, due to a central spine. In one region, the antecubital fossa, the papules resemble atypical lichen planus, and it is probable that at a later date typical lichen planus will develop in other situations.

A number of similar cases have recently been exhibited at the Section by Drs. Barber, Dowling, and Graham Little, and by myself, and their inclusion within the group of lichen planus is now generally admitted.

It is interesting to note that the spiny eruption does not follow the distribution of lichen planus, that it is characteristically found in patches on the trunk, and occasionally on the scalp, where it may be accompanied by genuine atrophic areas, resembling pseudo-pelada. I am not aware that in the "spiny" stage the disease has previously been observed on the mucous membranes, although genuine lichen planus may occur in this situation in the mixed forms.

Discussion.—Dr. DOUGLAS HEATH said he dissented from the view that these cases should be labelled lichen planus. Any toxic condition might cause a certain amount of follicular upraising. A tuberculide on the body might look spinous, and then flatten down, as in the case which Dr. O'Donovan had recently shown before the Section. He thought the papules in the present case had not the characters of lichen planus. If one scratched a lichen planus area, a feeling of substance was imparted to the nail; but the lesions in this

case could be picked out, leaving a raw surface. In this case there were little groups of bright red papules, particularly in the groins and the axillæ, an unusual distribution for lichen planus. Again, the lesions in front of the denture were what one would expect from any ill-fitting denture. Seborrhœic eruptions often had a central distribution, as in the case of this woman, on the front of the chest and between the shoulders. If a seborrhœic person had an infection of a nasal sinus, or an acute catarrhal condition of the nose or throat, all the old lesions might become activated and raised up again. He knew that in cases of lichen planus there was frequently a somewhat inflammatory papule, but many people thought that if a rash showed a tendency towards a spinous character, the case was bound to become one of lichen planus later on. He would like to see some of these cases at a later stage, to test the truth of that opinion. Many of the seborrhœic cases had a lichen-like phase, so had other skin diseases. He had recently seen a case of lupus erythematosus with a typical symmetrical "butterfly" diffuse eruption on the face, with lichenoid papules of the lichen planus type over the limbs and elsewhere.

He therefore thought there was an unwise grouping of these conditions. A lichenoid phase could be seen in a large group of eruptions, and it was incorrect, he thought, to label these eruptions lichen planus.

Dr. MACCORMAC (in reply) said that he had now seen a number of similar cases. Two in his private practice had begun in the same way, and both had at a later stage developed typical lichen planus. He believed that the majority, if not every example of this eruption, as seen in the adult, belonged to the lichen planus group, and that in this respect they differed from the lichen spinulosus of childhood.

Section of Anæsthetics.

[*December* 6, 1929.]

OPENING PAPERS IN A DISCUSSION ON ANÆSTHESIA IN RECTAL SURGERY.

I.—Dr. J. K. Hasler.

THE branch of surgery which deals with the rectum is one which is particularly satisfactory from the standpoint of the anæsthetist. If he elects to give a general anæsthetic his administrations are well out of the way of the surgeon, and if a local or regional one is desired, he is dealing with an area of the body which is well adapted for that type of anæsthesia. Moreover, apart from the operations for the removal of cancer of the rectum, the operations are seldom productive of much shock, nor is the anæsthetist often worried with a patient *in extremis*.

Rectal operations fall conveniently into two groups: those which are performed from the abdomen and those from the perinæum. I propose to deal with these two groups separately and to discuss the forms of anæsthesia which may be used for each group.

Abdominal Operations.

Starting with the smaller group, the operations performed from the abdomen, we find that they are almost entirely to deal with some form of malignant disease connected with the rectum. Probably more than half are for the operation of colostomy, the others being either for the abdominal resection of a growth as in Coffey's operation and abdomino-perinæal excision, or for the insertion of radium into a high growth of the rectum and the glands associated with it.

The requirements of the surgeon who is performing these operations are much the same as for any other form of abdominal surgery. Firstly, there must be good relaxation of the patient's abdomen, so that unnecessary coils of intestine are not constantly being forced through the wound. Secondly, the patient must be sufficiently anæsthetized to enable the surgeon to explore the abdomen if he desires to do so, and to determine the presence or absence of secondary malignant deposits in the liver. In addition it must be borne in mind that, for colostomy in particular, the operation is often the first of two, and the patient must be kept fit for a second operation in ten days' or a fortnight's time.

A good general anæsthetic will satisfy these requirements, and it is impossible to say that any of them is necessarily the best. Each anæsthetist, and to a lesser extent each surgeon, will have his own individual preference. A general practitioner working in a country cottage hospital will probably give a more satisfactory anæsthetic with a chloroform and ether mixture on an open mask than he would with a gas-and-oxygen machine, and I believe that each anæsthetist should use the anæsthetic which will enable him to give the best results. A common procedure is to administer a general anæsthetic for the preliminary colostomy, and a spinal anæsthetic, combined with some form of twilight sleep, or a light general anæsthetic, for the subsequent perinæal excision. The method is satisfactory, but there is no reason why general anæsthesia should be employed at all. The surgeon's attentions are mainly confined to the lower half of the abdomen, and a spinal

anæsthetic injected between the third and fourth lumbar vertebræ will produce anæsthesia well above the umbilicus, besides giving good relaxation to the abdominal muscles.

It is perhaps worth while to mention that the giving of a spinal anæsthetic will not necessarily prevent chest complications. I gave spinals to two cases of prostatectomy during the early part of this year, both of whom suffered with severe chest complications afterwards. In one case the patient developed a severe bronchitis which nearly proved fatal, and in the other case there was a recrudescence of pulmonary tuberculosis. It seems reasonable to suppose, however, that these patients would have been worse off after a general anæsthetic, and I think that there should be no hesitation in giving a spinal anæsthetic in preference to a general if there is any reason to worry about the patient's chest.

Perinæal Operations.

Turning to the larger group of rectal operations—those performed from the perinæum—we find the field for anæsthesia much more varied and interesting. Before dealing with the subject of general anæsthesia for these patients, I should like to say a word about their psychology. The three common complaints from which they suffer are hæmorrhoids, fissure, and fistula. These are all chronic complaints which may, and often do, cause varying degrees of pain and anxiety for many years before the patient summons up his courage to undergo surgical treatment. Nor can these conditions be openly talked of with his friends in order to elicit sympathy. To the lay mind the operation of appendicectomy is a respectable proceeding, but a certain loss of dignity is associated with having one's piles cut off. Consequently they suffer in solitude, and when they arrive at the operating theatre they are nervous and irritable and do not take kindly to the anæsthetic. Many of them begin to resist as soon as the stage of unconsciousness is reached, and with many the state of relaxation is longer in coming. In addition, a large number of these patients belong to a type which may best be described as "tough," and of which good examples are shown by the cab-driver, or the railway porter, with a regular fondness for alcohol. Therefore these patients require to be deeply under before the surgeon can begin his work, especially as the perinæal reflexes are among the last to disappear under general anæsthesia. Otherwise there may be reflex contraction of the leg muscles which will prevent the patient from being placed in the lithotomy position, or, if he is already there, will push him out of it. That is especially apt to happen when the sphincter is forcibly dilated. It follows, then, that whatever the general anæsthetic, it must be given liberally, at any rate at the commencement of the operation and until good relaxation has taken place. There is one exception to this statement, namely, pure chloroform. Chloroform is widely condemned for operations which involve the anus and the sphincters of the rectum. If the patient should happen to be insufficiently anæsthetized with chloroform when the surgeon dilates the anus, there is, first, a risk of cardiac inhibition through the vagus, with its unpleasant consequences, and, second, there may be reflex inhibition of respiration or laryngeal spasm, which, with its accompanying cyanosis, is undesirable in the presence of chloroform.

Professor Yeomans, of New York, in his volume on proctology, states that general anæsthesia is indicated in children, in nervous individuals who may prefer it, occasionally to obtain complete relaxation for diagnostic examination, and for the performance of certain operations, notably incision of abscesses situated above the pelvic diaphragm, complicated fistulæ, cancer of the rectum and pelvic colon, and other operations on the sigmoid. He considers that chloroform has no place in rectal surgery, and that gas-and-oxygen is chiefly useful for minor surgical procedures such as opening abscesses and dilating the anus and for removing the packing in a deep wound.

Local Anæsthetics.

The local anæsthetics used for perinæal operations in rectal surgery can be classified under three headings. First, there is the anæsthesia produced by local infiltration of the area of operation; second, there is extradural anæsthesia which is produced by caudal and sacral blocks; and third, there is intradural, or various forms of spinal anæsthesia.

Local Infiltration.—In the local infiltration method 20 to 30 c.c. of the anæsthetic fluid, commonly a 1% solution of novocain, are injected round the outside of the rectum at a depth of about 2 in. from the surface. A preliminary wheal is raised in the skin just posterior to the anus and in the mid-line. Through this wheal is introduced a longer needle, and, with a guiding finger in the rectum, 10 c.c. of novocain are injected posteriorly. The needle, still piercing the wheal, is then moved round to the sides and front of the rectum and 5 c.c. are injected on either side. As an alternative method the needle may be introduced through the wheal and a ring of novocain injected subcutaneously round the anus. Four injections of 5 c.c. each are then made through this ring at the four cardinal points of the compass. Within five minutes the sphincters should be relaxed and anæsthesia be present. Local infiltration provides a satisfactory anæsthesia for the treatment of hæmorrhoids, but does not give a large enough area of anæsthesia for fistulæ which often spread well into the buttock.

Extradural Anæsthesia.—The extradural methods of producing anæsthesia for operations on the rectum and anus are by means of a caudal block, a trans-sacral block, or a combination of the two known as a sacral block. These are methods which have enjoyed greater popularity in America than in this country.

In caudal block a certain quantity of anæsthetic fluid is injected through the sacral hiatus into the caudal canal. The quantity to be injected is recommended as 30 to 40 c.c. of a 2% solution of novocain, but some prefer to use a greater bulk of a weaker solution. It produces a satisfactory anæsthesia if it works properly. Unfortunately there is a certain percentage of cases in which anæsthesia remains absent, and also it takes from fifteen to thirty minutes or even longer before the anæsthesia is complete. During the early part of this year I employed tutocain for this purpose. Tutocain is a local anæsthetic which is said to be about one third as toxic as cocaine and twice as toxic as novocain. When using 20 c.c. of a 2% solution I found that anæsthesia could be obtained within ten minutes. The anæsthesia was deeper than is obtained with novocain, and deep pressure sensation appeared to be absent. Unfortunately there were the usual percentage of failures even in thin subjects in which the injection into the canal presented no difficulty. Another drawback to caudal block lies in the fact that it is difficult to make the injection a completely painless one, and patients are apt to become resentful if the anæsthetic fails to act after they have been put to a certain amount of inconvenience.

In America the caudal block is often combined with a trans-sacral block. This consists in injecting the anæsthetic solution into the sacral foramina on each side starting with 6 c.c. into each first foramen, 5 c.c. into each second foramen, and so on. Dr. J. S. Lundy, who has considerable experience of this method at the Mayo Clinic, states that intense anæsthesia should be present about ten to fifteen minutes after the injection is completed, and that it should last for two hours. He records 99% of successful cases among the smaller rectal operations, and 75% to 85% of successes in cases of carcinoma of the rectum. Two others recorded only three failures in a series of 225 cases. It appears to me to have certain drawbacks, however. On the occasions on which I practised trans-sacral block in the post-mortem room I found it none too easy to locate the foramina with the needle, and usually managed to come up against bone. This must surely prove painful for the patient, and, moreover, the giving of eight to ten injections would take as long, if

not longer, than an operation for hæmorrhoids or fissure unless the anæsthetist were particularly skilled at it. I imagine that much constant practice would be necessary before one could become skilful in its performance, and be justified in using this method.

Referring to extradural anæsthesia Professor Yeomans says that the anæsthesia following a trans-sacral block sets in almost immediately. It lasts generally from two to four hours and is decidedly more certain and constant in its distribution than caudal block alone. These definite advantages justify a combination of caudal and trans-sacral block inasmuch as the latter entails but little additional risk. Proficiency in sacral anæsthesia can be acquired only by careful study of the sacrum and its anomalies, and practice on the cadaver in locating the sacral foramina.

Intradural Anæsthesia.—Intradural or spinal anæsthesia is now sufficiently well established not to require any description. Its advantages and disadvantages were discussed in this Section not long ago. In cases of cancer of the rectum it is a particularly valuable form of anæsthesia when combined with either a light general anæsthetic or with some form of twilight sleep. If an injection consisting of morphia, gr. $\frac{1}{4}$, and scopolamine gr. $\frac{1}{150}$ is given from half to three-quarters of an hour before the operation, the patient will usually drowse or sleep as soon as the spinal anæsthetic has been given and he has been made comfortable in the left lateral position. If necessary a second, and smaller, dose of scopolamine can be given when he arrives at the theatre. Under these conditions a general anæsthetic can be dispensed with altogether. It occasionally happens that with a high growth of the rectum some traction must be exerted on the bowel in order to bring the growth down. The inevitable tugging on the mesentery may wake the patient and cause him to complain of pain in the abdomen. When this happens some general anæsthetic is unavoidable. Gas-and-oxygen may be given until the difficult part of the operation is completed, or a little chloroform and ether mixture on an open mask. This latter anæsthetic usually has the effect of sending the patient off to sleep again without the necessity for full surgical anæsthesia, and the absolute minimum is required to keep him there.

While a spinal anæsthetic does sometimes produce anæsthesia lasting from one and a half to two hours, it can only be relied upon to last for one hour with any degree of certainty. If there is any reason to suppose that the operation will be unusually difficult and last for one and a half hours or more, the spinal may be combined with a caudal block. This extra injection takes up very little time and has the effect of prolonging the duration of anæsthesia.

For the smaller rectal operations a spinal anæsthetic is somewhat cumbersome to use as a routine. The area of operation is limited to the perinæum and no surgeon wants anæsthesia reaching to the umbilicus for it. In addition there is the accompanying fall in blood-pressure and occasional nausea and sweating. The ideal spinal anæsthetic for these smaller rectal operations would appear to be one whose action could be limited to the sacral nerves, thus producing a perinæal anæsthesia and avoiding a fall in blood-pressure. This "low spinal," as it may be conveniently termed, can be easily produced by injecting the fluid between the fourth and fifth lumbar vertebræ with the patient in the sitting position and letting him remain there for about two minutes. If the anæsthetic solution is injected into the spinal canal very slowly to avoid undue mixing with the cerebrospinal fluid, it will sink to the bottom of the dura mater and act only on the lowest sacral nerves. When the injection is completed the patient should be made to sit up straight for about two minutes, after which he can lie down and be wheeled into the theatre.

I have been using this method at St. Mark's Hospital for several months now and the solution employed has been 10% stovaine in saline (stovaine-billon). This is usually called the "light" solution as opposed to the "heavy" solution which contains stovaine in glucose. It seems conclusive that the light solution is heavier

than the cerebrospinal fluid, and that gravity plays an important part in the distribution of anæsthesia. Besides producing a low spinal anæsthesia with the patient in a sitting position, this fact can be also demonstrated by leaving the patient on his side after injection when a unilateral anæsthesia can be produced with the anæsthesia on the side on which the patient is lying. The amount of solution injected has usually been about 0·5 c.c. or 0·6 c.c. Sometimes it is only the fourth and fifth sacral nerves that are affected but in most cases the third sacral is affected as well. It is not necessary to mix the stovaine with its own bulk of cerebrospinal fluid though I have usually done so in cases of fistula where the area of operation is larger than in cases of hæmorrhoids and fissure. So far about fifty cases have been anæsthetized in this way, and the effect on the patient at the time of operation has proved satisfactory. There does not appear to be any fall in blood-pressure, and attacks of nausea and vomiting have been absent. The low spinal, however, does not prevent the bladder trouble which sometimes follows the giving of a spinal anæsthetic, and several of the patients have required to be catheterized for two or three days after operation.

The recent papers by Drs. Pitkin and Kelly suggest that spinocain would be a useful anæsthetic for producing a purely perinæal anæsthesia. By tilting the patient's body either up or down, according to whether the heavy or the light solution has been used, the anæsthetic effect can be limited to the pelvic region. I cannot claim to have had any practical experience with it, but an examination of the literature on the subject suggests one drawback, viz., the risk of altering the patient's position relative to the horizontal plane for at least two hours after operation. I do not know how real an objection this is, but it could probably be minimized by using a smaller quantity of spinocain. When only just over 0·5 c.c. of stovaine is used, this objection is non-existent, as the stovaine is quickly fixed, and the subsequent position of the patient does not matter as far as the anæsthetic is concerned.

One word with regard to local anæsthetics in cases of fistula. It is not always desirable to produce full relaxation of the sphincters in cases of fistula, especially if they happen to be extensive. In such cases it is usually imperative for the surgeon to be able to feel the sphincters easily while operating. Local anæsthetics, and particularly spinals, relax the sphincters to such an extent that this may be difficult or impossible, and therefore a general anæsthetic is often preferred. I am not sure whether this is altogether true with the low spinals, as some of the cases which I have anæsthetized in this way have seemed to be only partially relaxed.

On the subject of rectal anæsthetics in rectal surgery I do not feel qualified to speak as I have no experience. The recent tests with avertin in this country included some cases for the ligature of piles, and the results appeared to be quite satisfactory, so there seems to be no serious contra-indication to their use.

The operations on the rectum are sometimes thought to be a rather uninteresting branch of surgery. In the foregoing remarks I have tried to show briefly that there is more variation in the methods at the disposal of the anæsthetist than is apparent at first sight. If I have dwelt on local—rather than on general anæsthetics—it is because I think they are apt to be overlooked in a class of operation for which they are well suited, and also because there is a growing tendency at the present time to avoid a general anæsthetic if a satisfactory alternative can be found.

II.—Mr. E. T. C. Milligan.

Till recently the value of an anæsthetic for hæmorrhoidectomy was considered enhanced if it could ensure relaxation of the sphincter ani, indeed, if it did not, the surgeon proceeded to stretch the sphincter forcibly in order to expose the piles, a procedure to which both patient and anæsthetist reacted, but in different ways.

Now, of course, as hæmorrhoids are withdrawn from the anus and exposed by

dissecting forceps, relaxation of the sphincter ani is immaterial, and therefore the ideal anæsthetic for hæmorrhoidectomy need not be one which produces relaxation of the sphincters.

On the other hand, when operating on extensive fistulæ, in which the internal opening in relation to the internal sphincter has not been determined beforehand, it is important to feel tightly gripping sphincters, so that the upper limit of the internal sphincter in relation to the internal opening and ramifications of the fistula can be visualized. Incontinence, through cutting the upper part of the internal sphincter, is thus avoided.

In this class of case an anæsthetic which causes relaxation of the sphincters is bad. This condemnation, however, does not hold with regard to simple fistulæ in which the relations of the internal opening and the track to the sphincter ani are simple and have been determined beforehand.

The operations for fissure, fistulæ and piles, are almost technically perfect. Complications have been practically banished, simplicity of technique has been attained, and permanent and satisfactory cure is the rule.

In comparison the anæsthetic appears to assume perhaps more importance to the patients' well-being and comfort than the actual operation. It is therefore a desirable and promising field for endeavour to improve our anæsthetic methods. The ideal for pursuit is to abolish apprehension before the operation, to banish pain and apprehension during, and to eliminate pain afterwards. To these ends in rectal operations Mr. Hasler and I have directed our interest.

He has given an account of the various methods employed. Our investigations still continue, but I may perhaps be allowed to record impressions up to date.

Caudal Block Anæsthesia—although, if reliable, it would be ideal—is uncertain and unreliable. With identical technique the results vary in individual cases from perfect perinæal anæsthesia, through partial anæsthesia when the distress of the patient during operation is great, to absence of anæsthesia, when another anæsthetic has to be substituted.

It has the advantage of easy administration, but has also the decided drawback that such administration is not always pleasant to the patient. There are no unpleasant after-affects.

Local Anæsthesia.—Several satisfactory techniques can be employed, all depending on the recognition by palpation of local anatomical landmarks.

Thus the operator is the one best fitted to carry out the injection.

Theoretically, local injections in this particular region should carry infection into these vulnerable tissues, but in practice infection is almost unknown.

Local anæsthesia is, in hæmorrhoidectomy, one of the best anæsthetics from the operator's standpoint, and also for the welfare and comfort of some patients, but there are many patients who are apprehensive from first to last, in whom the mere sensation of manipulation commonly felt is interpreted as "feeling the whole of the operation." The patients feel that something unknown and probably painful is being carried out in a part to which their mind has been painfully directed daily—sometimes all day—perhaps for years. It is no wonder that some patients wish consciousness of any manipulation "blanked out" while the operation on this misery-producing part is being performed.

Perhaps the pleasantest and best way of "blanking out" consciousness of the whole episode, as well as of pain during these rapid and simple operations, is by gas-and-oxygen anæsthesia with preliminary sedative medication.

Low spinal or spinal anæsthesia limited to sacral nerves has advantages which render it of the greatest value for operations on the perinæum.

It is reliable. Sensation is completely abolished in the field of operation, and further, the anæsthesia is restricted to this field, so that the patient is quite unconscious of any manipulations in the part and no apprehension is felt.

It is a controllable anæsthetic and has none of the disadvantages of the higher spinal anæsthetics.

There is no feeling of paralysis in the legs; the blood-pressure is unaffected. Unpleasant bladder sequelæ do not occur, and there is no complaint of headache.

The administration of the anæsthetic is simple and is quickly carried out. It is not unpleasant to the patient and is convenient to the administrator if he is skilled in the technique. Anæsthesia is complete in two or three minutes. Apprehension before operation can be abolished by sedative injections.

For hospital work it is ideal. Most of the bad results following spinal anæsthesia are due to improper selection of cases and faulty technique.

The technique of spinal anæsthesia is simple, but it must be carried out with the minutest exactitude and attention to detail.

Pain after rectal operations is a variable quantity; some patients have none, others have a little, and others have a great deal, necessitating sedative drugs for a short time. Post-operative pain bears no relation to the method of anæsthesia.

[Other speakers in the discussion were: Dr. H. L. FLEMMING, Dr. HOWARD JONES, Dr. C. F. HADFIELD, Mr. FRANKIS EVANS, Mr. R. E. APPERLY, Dr. H. CRAMPTON, and Mr. TURNER WARWICK.]

Clinical Section.

[*December* 13, 1929.]

Dystrophia Myotonica.—C. WORSTER-DROUGHT, M.D.

A. E. D., male, aged 34. Complains of (1) stiffness in hands, i.e., difficulty in extending fingers after flexion; (2) stiffness in legs and back on attempting to walk after sitting; (3) stiffness in the lower jaw, causing difficulty in eating and speaking.

History.—No previous illness. Enlisted in infantry in 1917 and passed successfully through military training, handling a rifle satisfactorily. After eleven months' service in France began to experience difficulty in manipulating his rifle owing to apparent stiffness of hands. Contracted diphtheria and was invalided home. Discharged from the Army in 1919. Since that time has become considerably thinner and stiffness has developed in back, legs and lower jaw.

Family History.—No similar disorder can be traced. Father died aged 74; developed cataract at age of 60. Patient is seventh of eleven children. Has had three children, two died in infancy; the remaining child, aged 14, is well. Apart from patient's father no member of family has had cataract.

Condition on Examination.—The main features include: General muscular atrophy, especially of arms, with temporal and malar hollowing; premature baldness; active myotonia mainly in masseters, flexors of wrist and fingers, and erector spinæ; reactive myotonia in many other muscles; myotonic electrical reactions in affected muscles; absent knee- and ankle-jerks and some testicular atrophy.

Pupils equal, react sluggishly to light but normally to accommodation. Tendency to double ptosis, with compensatory spasm of occipito-frontalis; myopathic facies, with diminution in lines of expression and temporal and malar hollowing. Speech is thick, occasionally slurred and indistinct.

The following muscles show active myotonia: masseters, erector spinæ, peronei and muscles of calf. Slight active myotonia is also present in sterno-mastoids, deltoids, biceps, extensors of wrists and fingers, quadriceps, hamstrings, extensors and flexors of toes. Reactive myotonia only is present in trapezii, pectorals, triceps and anterior tibial muscles.

Reflexes: Supinator, biceps and triceps jerks present, but sustained; wrist-jerks absent; abdominal reflexes sluggish; knee and ankle jerks absent; plantar reflexes flexor.

Coördination: Slight incoördination of arms, left more so than right. No tremors.

Sensation: Deep sensation impaired in legs.

Trophic changes: Premature frontal and vertical baldness. Testicles soft and somewhat atrophic, left more so than right.

Other systems: Bradycardia, pulse averaging 48; heart otherwise normal. Blood-pressure: 115/75. Remaining systems normal.

This rare disease has been regarded by some authors as a polyglandular endocrinopathy. In one or two cases examined post-mortem, changes have been described in the pars anterior and the pars intermedia of the pituitary body, and in the cortex of the suprarenal gland. Microscopically, the myotonic muscles show no abnormality, but the atrophic muscles show atrophy of some of the fibres. The blood chemistry in the present case has been shown to be normal. The only blood abnormality I have found in a few other cases is a relative mononuclear leucocytosis and an occasional slight eosinophilia. The calcium, phosphorus, glucose and other constituents of the blood are normal.

Tuberculous Ulceration of the Tongue.—PHILIP TURNER, M.S.

George C., aged 48, admitted to hospital for ulceration of tongue.

Past History.—Treated at sanatorium five years ago for tuberculous disease of lung. Four years ago admitted to hospital on account of ulcer of buccal surface of left cheek

just behind angle of mouth. This was excised, and on histological examination proved to be tuberculous. It was three-quarters of an inch in diameter, and it looked like an epithelioma, but was so remarkably soft that on pressure it could scarcely be felt at all. It has healed up very well, and there has been no further trouble.

The present trouble began about eighteen months ago, and the ulcer has gradually increased in size and extent. There has been little or no pain, no tenderness on touching the tongue and no discomfort on taking food. On the dorsum of the tongue there is a raised area about 1½ in. by ½ in. This is bounded by a deep sulcus which, if opened, shows ulceration at its base. There is also a definite area of ulceration at the back of the groove. There is some induration behind but little or none at other parts of the sulcus. At the left side of the tongue are two small indurated nodules, the posterior of which is ulcerated. The latter was excised December 6, 1929, and histological examination shows it to be tuberculous. The lymphatic glands on both sides of the neck are slightly enlarged. There are signs of phthisis on both sides of the chest and an X-ray examination shows that there is extensive tuberculous disease of both lungs.

There is no tuberculous disease of the larynx. The patient was in a sanatorium some years ago, and the phthisis is not at present active. There are no symptoms, and the tongue has been very much the same for the last year. I do not propose any active treatment, as it might light up the pulmonary tuberculosis; the ulcer will be kept clean, and the patient's general health will be maintained as far as possible.

Discussion.—Dr. R. RUTHERFORD asked what treatment Mr. Turner proposed to apply to the ulcer on the tongue.

Mr. TURNER (in reply) said that the treatment of the tongue was very simple: consisting merely of a potassium chlorate mouth-wash, and the application of glycerine and borax.

Polycythæmia Vera Treated with Phenylhydrazine. — TERENCE EAST, M.D.

Male, aged 52. Came to hospital complaining of pain and discoloration of a toe, which had been troublesome for some months. Headache and giddiness for some months, but not severe.

Pulsation in tibials poor. Arteries rather thick. Blood-pressure 160/115.

Distinct cyanosis. Spleen just palpable. No cardiac enlargement. Wassermann reaction negative. Urine normal; urea-concentration normal. Fragility curve showed that the red cells were a little more fragile than normal.

After six weeks in hospital under treatment, the blood-pressure settled at 100/75. The spleen was no longer palpable. Later, as the blood-count rose again to a high level, the blood-pressure was 135/100, and the spleen was again felt.

The charts show the effect of treatment with phenylhydrazine hydrochloride on the blood-picture and on the blood-bilirubin. [Charts demonstrated on screen.]

At present the patient feels well and has no symptoms, and I would like to know whether we should continue to give small doses, or wait until symptoms appear and then give moderately large doses. Phenylhydrazine is probably a poisonous drug and may have a bad effect on the liver. I think the administration of moderate doses from time to time is better than one or two large doses. The blood-pressure was originally high (160/115) but fell with the changes in the blood picture. It has risen again, but not to such a height.

Discussion.—Dr. F. PARKES WEBER said he had at present two cases of the kind under this treatment, but as yet it was too early to judge of the results. Two other recent cases had had complications which had prevented him from trying phenylhydrazine treatment. One had considerable jaundice of the acholuric kind, and he thought that destroying more red cells by phenylhydrazine, instead of removing them from the body by bleeding, would

throw extra work on the liver, and so favour the development of bilirubin-calculi and even hepatic cirrhosis.[1] In the other case there was decided albuminuria, and in consequence of that the drug had not been tried. He found, however, that the last patient was now being given benzol internally at another hospital.

The fall in blood-pressure following phenylhydrazine treatment in Dr. East's case was very interesting if confirmed by similar results in other cases.

Dr. EVAN BEDFORD said he had treated two cases with this drug, and his impression also was that it reduced the number of red cells. One of his own patients had had jaundice, and the doses given had been comparable with those given by Dr. East. Did Dr. East consider that the jaundice was due to hæmolysis, or to a toxic action of the drug on the liver cells? If due to hæmolysis, it was not necessarily very serious, but if due to a toxic effect on the liver, the patient might be very ill. His own patient had appeared to be very ill at the time.

Dr. H. STANNUS asked whether hæmoglobinæmia had occurred, and if so, whether determinations were made of the amount after the drug was given, and also whether hæmoglobinuria was present. These cases were of importance to tropical medicine, as they had a bearing on the question of the production of blackwater fever in malaria.

Dr. H. V. MORLOCK said he had seen one case treated by Dr. Scott Pinchin in this way, and during the treatment the blood-count had fallen, but it had afterwards risen again. The patient had been better while taking the drug and for some weeks afterwards, but he had not continued its use because, though there had been no jaundice, he was afraid of damage to the liver.

Dr. E. STOLKIND said he had treated a case of erythræmia for eight years, and had tried most of the classical methods of treatment, including potassium iodide, benzol, blood-letting, etc. At the beginning the red cells were 10,000,000, hæmoglobin 150%. Finally, he resorted to deep X-ray therapy, and this resulted in the reduction of the red cells to between six and seven million, the colour-index being 0·78.

Dr. MICHAEL ALBURY said that in using a drug of such potency it was important to know what were the earlier and delicate manifestations of its toxicity. A brisk rise in the polymorphonuclear cell count was taken to indicate a toxic effect on the liver, and therefore the discontinuance of the drug. Albuminuria in patients with hypertension was of doubtful significance. The smallest dose which he himself had used was 0·45 grm. He had seen a few cases in which a daily dose of 0·1 grm. had been given over one or two weeks, the patient's progress being carefully controlled by the fall in the red cell count, and also by observing the level of the white cell count.

Dr. TERENCE EAST (in reply) said that with regard to the increase of bilirubin in the blood there was only an indirect reaction. He did not know how one could say whether the increase in the pigment was simply due to the broken-down red cells, or whether it indicated damage to the liver. The highest level for the van den Bergh, three units, came very soon after giving the drug. Probably the increase in the blood bilirubin was partly due to the toxic effect on the liver. It was curious that the bilirubin should have been so low before treatment—0·2—when the patient had so much in the way of red cells, which must have been continually breaking down. The dark colour of the urine was due to urobilin, not to bile. There had been no hæmoglobin in the urine.

Severe Rickets with (?) Dyschondroplasia.—BERNARD E. MYERS, C.M.G., M.D., and ST. J. D. BUXTON, F.R.C.S.

G. B., male, previously shown before this Section.[2]

He can now walk and is much more healthy. Ossification of all the long bones is proceeding satisfactorily. There is a well-formed epiphysis for the head of the femur and the deformities at the end of the bones are greatly diminished.

Coxa vara is still present—greater in one leg than the other.

The diagnosis is still open to question, but it is considered that rickets is the cause of the greater part of the condition.

1 F. Parkes Weber, "Erythræmia with a High Degree of Acholuric Jaundice," *Brit. Med. Journ.* 1929 (ii), p. 892. The jaundice, though acholuric, was not associated with abnormal fragility of erythrocytes.

2 *Proc. Roy. Soc. Med.*, 1929, xxii, 399 (Clin. Sect., 21).

[The progress of the case by radiograph was demonstrated.]

In the South of England we see little severe rickets. Is this condition entirely due to that disease, or is there also some condition of dyschondroplasia or other bone disease in which there is irregularity of ossification?

Discussion.—Dr. M. ALBURY asked whether in this patient there was any abnormality in renal function, particularly if there had been any azotæmia.

Mr. ST. J. D. BUXTON (in reply) said that all examinations of the kidney showed normal function.

Familial Acholuric Jaundice (Son, Mother and Grandmother).—H. V. MORLOCK, M.D.

Boy, aged 8, admitted to hospital complaining of pain in left side of abdomen. During last month has had attacks of colicky pain in left hypochondrium. No other symptoms complained of.

On Examination.—Delicate-looking boy. Slight icteric tinge of conjunctivæ. Heart and lungs normal. Spleen palpable 3 in. below costal margin. Urine: Bile salts and pigments absent; urobilin present.

Blood-count: Red cells 5,100,000, hæmoglobin 60%, colour-index 0·6. White cells 16,800 (*Differential:* polymorphonuclears 70%, lymphocytes 22%, large mononuclears 6%, eosinophils 2%).

No abnormal red or white cells. Slight anisocytosis and poikilocytosis.

Fragility test: Hæmolysis commences at 0·7% and is complete at 0·5%. Control commenced at 0·45% and was complete at 0·30%.

Van den Bergh reaction: Direct negative; indirect positive. Wassermann reaction negative.

Three years ago the child's blood showed no abnormal fragility. His mother, aged 32, has been known to have the disease for fourteen years; her spleen is enlarged, but she refuses to have splenectomy performed. The child's grandmother, aged 65, has been known to have the disease thirty years; her spleen is greatly enlarged, but she also refuses to have splenectomy performed. The child's grandmother's brother was known to have the disease, but died at the age of 36; the cause of death is not definitely known.

Discussion.—The PRESIDENT said it would be agreed that the child's spleen had better be removed, but he would like to know whether Dr. Morlock really thought it desirable to advise splenectomy for the grandmother also.

Dr. TERENCE EAST said that, since three years ago this child's corpuscles had no abnormal fragility, he wondered to what extent was this a congenital case. In a sense it was an acquired condition directly from birth.

Dr. F. PARKES WEBER said that all cases of familial hæmolytic jaundice and the congenital isolated cases of the same nature could be roughly divided into two groups: (1) the chiefly icteric, and (2) the chiefly anæmic; examples of both groups could occur in the same family. Usually cases of the first group did very well, excepting that they often ultimately showed a tendency to the formation of bilirubin calculi in the liver. The "anæmic" cases were the ailing ones. Dr. Morlock's cases belonged to the icteric group, and so did most of the familial series studied by Dr. Dorner and himself in 1909.[1] In that series the grandfather, who had been jaundiced all his life, had lived to the age of 76 (wrongly given as 70 in the published account).

Dr. MICHAEL ALBURY said that the treatment indicated in this case seemed to be splenectomy. From the technical point of view the operation would be a simple one, as there was no thickening of the splenic capsule and no infarction, in marked contrast to cases of splenic anæmia in which there was perisplenitis, and leashes of collateral venous circulation which tethered the organ. These patients went through periods when they were well and then became incapacitated by a hæmolytic crisis, and as this event might be precipitated by any trivial infection, the patients' lives were rendered less useful by this disability. He

[1] F. Parkes Weber and G. Dorner, *Lancet*, 1910 (i), p. 227.

considered, therefore, that splenectomy should be performed in all these cases, preferably when the patients were young, an optimum period being about the age of this boy. When this child reached manhood and married, he would transmit the disease to his offspring, and it was a duty to warn acholuric parents that their children would be affected, and to advise them to have splenectomy performed at a suitable age. There was the danger, too, that such children might die in infancy, the reduction of the polycythæmia, which is physiological at birth, being associated with a fatal pathological crisis.

He thought that at the operation for splenectomy, exploration of the gall-bladder should be carried out as a routine, and that if pigment calculi were found they should be removed. It was doubtful if cholecystectomy should be performed in these cases since subsequent re-formation of calculi would constitute a grave danger.

Dr. DOROTHY HARE said she had watched a case after splenectomy for two and a half years. It was that of a woman aged 28. She had been much better at first, and though when seen a month ago, she had complained of feeling weak and easily tired, she had had no further jaundice; the fragility of her red cells had however not altered, so that, on the whole, the operation had been beneficial. She (the speaker) was at present watching the fragility of cells in the patient's child, a boy, now aged 4 years; a year ago they had been normal.

Dr. R. F. SMITH asked whether, if the spleen was removed, one could be certain that the child would not have acholuric jaundice.

Dr. MICHAEL ALBURY (in reply to Dr. Smith) said that the effect of splenectomy in these cases was to abolish the hæmolysis. The spleen was presumably hyper-active in acholuric jaundice. The inherent fragility of the red blood-corpuscles persisted, however, and did not return to normal after the operation, although it might decrease to a slight extent. Splenectomy, therefore, did not remove the inherent factor, and thus did not prevent the disease from being handed down to the next generation.

Dr. H. V. MORLOCK, in reply, said he thought that this child inherited the disease from his mother, because the fragility was so great, whereas in the acquired case it was of a much slighter degree. He had a brother and sister (twins), whom he (the speaker) had examined, and there was no enlargement of spleen in either. The mother objected to a blood-count being done because the child was of tender age. He was indebted to Dr. Albury for his advice; he now felt convinced that splenectomy ought to be performed. Dr. Albury had said that if bilirubin quickly appeared after removal of the gall-bladder and spleen, it would be a serious matter, and the speaker would like to know from him why it was serious.

Dr. ALBURY (in reply to Dr. Morlock) said that if pigment calculi were to form subsequently to the removal of the gall-bladder, the site of their formation would be the intra-hepatic ducts, and there would result a chronic obstructive jaundice, possibly with the development of cirrhosis, and, eventually, gross hepatic insufficiency with terminal cholæmia.

Combined Degeneration of Spinal Cord without Blood-picture of Pernicious Anæmia.—F. PARKES WEBER, M.D., and M. SCHOLTZ, M.D.

A. S., aged 39, tobacconist, was admitted to hospital on September 30, 1929, with spastic and slightly atactic gait, of gradual onset four years ago, together with paræsthesiæ (feeling of numbness and "pins and needles") in his lower limbs and lower front of trunk, and sexual impotence. Three months before admission he had occasional nocturnal and sometimes even diurnal enuresis. Patellar and Achilles reflexes exaggerated; ankle clonus obtained on left side, but on the right side only occasionally, and never sustained. Plantar reflex: of extensor type on both sides, but more easily obtained on left side. No definite anæsthesia anywhere, but apparently impairment of sensation for temperature in lower limbs. Cremasteric and superficial abdominal reflexes not obtained. Nothing abnormal in regard to upper limbs. Pupils react naturally. No nystagmus. Fundi normal. Slight Rombergism present. Wassermann reaction negative in blood-serum and cerebro-spinal fluid. Compression of jugular veins (Queckenstedt's test) produced increased flow of cerebrospinal fluid, which was normal in all respects. Complete gastric achlorhydria, by fractional tests, even after a subcutaneous injection of histamine (0·3 c.c. of an ampulla of "Imido," i.e., equivalent to about 0·0003 grm.); carmine-

fibrin test (Grützner) positive for the presence of pepsin. Urine: nothing abnormal. No enlargement of spleen or liver. No icteric tint of sclerotics. Blood-count (October 10, 1929): erythrocytes 5,280,000; hæmoglobin 86%; colour-index 0·83; white cells 5,300 (basophils 3%; polymorphonuclear neutrophils 58%; lymphocytes 36%; monocytes 3%). There is slight old bilateral deafness (otosclerosis).

Since October 14 the patient has been taking about 6 oz. of liver daily, and has been having an acid pepsin mixture with meals. There seems to be slight improvement in his nervous symptoms. Blood-count (December 4): erythrocytes 4,760,000, hæmoglobin 94%, colour-index 0·98, leucocytes 8,150.

Discussion.—Dr. PARKES WEBER said that histamin injections were sometimes valuable in cases of supposed gastric achlorhydria. In certain such cases during the fractional examination of the gastric contents free hydrochloric acid appeared after a minute subcutaneous injection of histamin. It was not known whether the absorption of histamin or a histamin-like substance from the intestinal contents normally acted as a stimulant to the acid-secreting ("oxyntic") cells of the stomach, but the question was interesting, as it might help to explain the frequent association of gastric hyperchlorhydria with habitual constipation.

The PRESIDENT asked for expressions of opinion as to whether treatment by liver had any effect on the spinal cord changes in conditions of this kind.

Dr. EVAN BEDFORD said he had under his care at the present time one of the first cases of pernicious anæmia to be treated with liver in this country, and while under treatment this patient had developed typical subacute combined degeneration of the spastic type, in spite of the fact that the red cell count was now 5,000,000. A point stressed by McAlpine was that the spastic type of this condition did not improve with liver treatment, though the other type might do so. He did not think that Dr. Parkes Weber's patient would improve as the result of treatment.

ADDENDUM (January 8, 1930).—No megalocytosis in patient's blood (Dr. F. E. Loewy). The Price-Jones curve is normal (Dr. L. J. Witts and Dr. J. Shackle). The blood-serum gives a negative direct, but a moderately positive indirect, Hijmans van den Bergh reaction for bilirubin.—F. P. W.

Specimen: Rheumatic Carditis, Pan-valvulitis.—HAROLD COOKSON, M.D.

Male, aged 22 at death; admitted to London Hospital, under Dr. John Parkinson, August 8, 1929.

History.—Scarlet fever at 12, rheumatic fever at 20; since this last illness he complained of shortness of breath, which was gradually increasing; three months before death, swelling of the feet occurred. For two and a half months before death the patient was under observation with congestive failure.

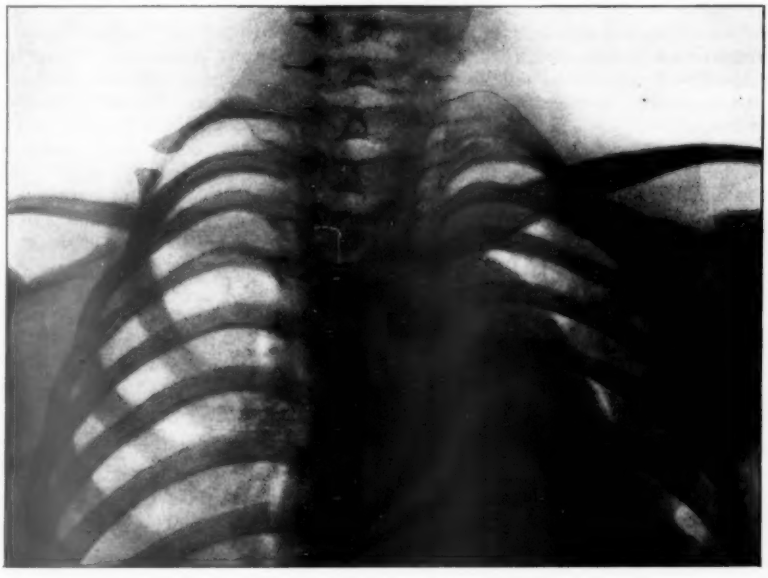
On Examination.—Apex beat in anterior axillary line, forcible, irregular (rhythm, auricular flutter). At the apex a systolic thrill was palpable; a systolic murmur and a rumbling diastolic murmur suggesting mitral stenosis were audible in addition to the heart sounds. To the right of the sternum in the fourth interspace there were a separate thrill and a rough murmur, both systolic in time. No diastolic murmur was audible at the base of the heart. The liver was enlarged and showed expansile pulsation, late systolic in time. Treatment with digitalis was badly tolerated, leading to coupled beats and vomiting, but having no effect on the auricular flutter. Patient died October 21, 1929.

Specimen.—All four valves are scarred by old rheumatic endocarditis, without recent vegetations. The tricuspid is thickened and retracted, especially its posterior cusp, producing some stenosis (circumference 8·8 cm.); the pulmonary exhibits thin ridges of thickening on the adjacent halves of two of its cusps; the aortic cusps show considerable fibrous thickening; the mitral is extremely stenosed, its buttonhole orifice measuring 1·6 cm. in length. The right auricle is greatly dilated; its wall shows focal hypertrophy, but other areas are thin and of a parchment-like

transparency. The left auricle is only slightly dilated, but is considerably hypertrophied. Both ventricles are considerably dilated and hypertrophied, more especially the right.

Chondroma of First Rib in a Child aged 5 Years.—CECIL P. G. WAKELEY, F.R.C.S.

There is a hard tumour on the right side under the clavicle, and attached to the cervical spine. The skiagram shows a first rib, with a cartilaginous defect in its centre; the tumour is purely cartilaginous, and is not shown by the X-rays (see figure).



Mr. Wakeley's case of chondroma of first rib.

I think that is where the chondroma is developing. There are no nerve symptoms, and the child shows no muscular weakness. I consider that the chondroma should be removed, because lesions of the brachial plexus due to cervical rib generally manifest themselves fairly late, and when they do appear, operation does not give excellent results; there is generally some permanent disability.

Congenital Morbus Cordis and Abdominal Tumour ? Causing Ascites.—D. C. HARE, C.B.E., M.D.

History.—I. B., female, aged 24, bookkeeper. Cardiac condition found on routine examination at school at age of 7. Games were then forbidden, but she now plays tennis, and has never been aware of any limitations due to her heart. Abdominal swelling with discomfort, but no pain, developed acutely from the beginning of October, 1929, and she was admitted to hospital October 24, 1929. Tendency to looseness of bowels; periods regular. No serious illnesses.

Family History.—A sister said to have heart trouble. No history of tuberculosis.

General Condition.—Nutrition good, complexion fresh, no cyanosis, no clubbing of fingers. No fever.

Circulatory System.—Pulse regular, 80 to 90. Heart enlarged; no præcordial bulging; widespread visible pulsation, especially at the base of the neck. Apex beat thrusting; no enlargement of veins. The apex is in the anterior axillary line in the fourth space, and the cardiac dullness extends about an inch to the right of the mid-line, and to the second left space above. Over the base are a thrill and "humming-top" murmur prolonged almost through the whole cycle, the maximum intensity being in the left second space. The murmur is widely conducted, but more to the left than the right. The first and second sounds are inaudible at the base, but forcible at the apex. Electrocardiograph report by Dr. Jenner Hoskin: A fairly physiological record with a left-sided preponderance.

Abdominal Condition.—On admission there was very great fluid distension, but no general or pulmonary œdema. Sixteen pints of fluid were removed, and examination suggested a mechanical, rather than an inflammatory, origin. After tapping, a large ill-defined mass was felt in the right lower abdomen extending across the mid-line, the note over the mass was dull. Skiagram shows displacement of intestines and of the stomach upwards and to the left. Pelvic examination is normal.

Special Examinations.—Wassermann reaction negative. Blood-count: red cells 5,500,000, hæmoglobin 84%, white cells 6,700.

The diagnosis suggested is a patent ductus arteriosus and an abdominal tumour with ascites unassociated with the cardiac condition.

[Electrocardiogram and skiagrams were shown.]

Discussion.—Dr. JENNER HOSKIN said that no doubt this was a case of congenital heart disease, and the murmur seemed to be typical of that of patent ductus arteriosus. There was a thrill more marked on the right side than on the left. The skiagram showed no transposition of blood-vessels. The two conditions in this patient were separate, and he did not think the heart condition was a cause of worry. The fluid in the abdomen was probably ascitic, rather than of the cystic type. Very likely there was tuberculous peritonitis. Laparotomy would be helpful. The abdomen had been aspirated and sixteen pints of fluid had been removed, but it was now re-filling. The patient looked fairly well.

Mr. CECIL WAKELEY said he considered that the abdominal condition was retroperitoneal, and his suggestion was that the patient was suffering from a retroperitoneal sarcoma. The skiagram was typically that of a retroperitoneal lipoma which was becoming sarcomatous. When the growth invaded the peritoneum, ascites was a most marked feature, and the case usually terminated within nine months. He advised opening the abdomen to confirm the diagnosis.

POSTSCRIPT.—An operation has been performed since the date of the meeting and the tumour was found to be an ovarian cyst with very lax walls. There was no solid tumour and no free ascites.—(D. C. H.)

Congenital Abnormality in the Shape of the Gall-bladder found by Cholecystography and at Operation.—E. STOLKIND, M.D.

G. L., male, aged 35, has had five severe attacks of pain in the right hypochondrium during the last eighteen months. Three of them were so painful that he thought he was dying. The last attack occurred about four months ago and lasted for two hours. After it he was very weak for about seven days.

In addition to these attacks he suffered from pain in the upper part of the abdomen, and for the last few months has had sickness and vomiting nearly every morning before breakfast on an empty stomach. In 1923 he underwent appendicectomy, and adhesions were found. There was no jaundice. He has, in addition, suffered from hystero-neurasthenia for many years.

Examination of Abdomen.—Tenderness on palpation in right hypochondrium. A point painful on pressure under lower rib near right mammillary line; tenderness in ileo-cæcal region on palpation.

All other organs normal.

X-ray Examination.—"The shadow of the gall-bladder after two doses of dye mass was very faint, and there is biloculation of the gall-bladder. The appearance suggests chronic cholecystitis with cholecystic adhesions."

On September, 27, 1929, Dr. H. Cecil Bull re-examined the patient at my request and reported: "The gall-bladder filled well, showing patency of the cystic duct. The outline was well rounded, but there was a peculiar constriction in the lower two-thirds of the gall-bladder. The shadow of the gall-bladder was of even density and there was no evidence of gall-stones . . . . The gall-bladder appears to indent the pyloric end of the stomach. It was not apparent when the patient was in the erect position . . . The shadow of the gall-bladder is normal, except for a constriction in its lower third."

The patient felt well while on strict diet and rest. But as he did not keep to the prescribed régime, he had frequent attacks of abdominal pain. On consultation with Mr. T. Twistington Higgins it was decided that there were adhesions and typhlitis in the abdomen, and an operation was performed on October 17. The omentum was extensively matted, and adherent to the structures in the lower right abdomen. These adhesions were divided, and considerable portions of the omentum containing large perforations were removed. Inflammation of the cæcum was observed.

The gall-bladder was of a peculiar shape, with an annular constriction of the fundus about two-thirds of its length down. No adhesions and no stones were found. There was no kind of obstruction to the passage of the bile.

In all probability this is a rare case of congenital malformation of the gall-bladder.

Mr. CECIL WAKELEY said that a number of cases of abnormality of the gall-bladder had been published since 1910, several under the title of "congenital annular gall-bladder." In the present case the surgeon appeared to have carried out an exploratory laparotomy and to have removed the omentum. He (the speaker) had published a case of double gall-bladder in the *British Journal of Surgery*[1] about three years ago

Tumour of Lung. Case for Diagnosis.—F. E. SAXBY WILLIS, M.D.

J. W., male, aged 50, porter. Admitted to Royal Chest Hospital November 22, 1929, complaining of stuffy feeling in chest and neck, and shortness of breath.

History.—Invalided from Army in 1900 with "emphysema." At that time had served in Malta and India. Complained then of cough and shortness of breath. Improved on his return to England. Rejoined Army 1914; wounded in right shoulder 1917, and at about that time again complained of cough and shortness of breath. These symptoms have become definitely worse during the last three months, being so troublesome in October, 1929, that patient was obliged to stop work, and (November 11) he came up to the hospital on the advice of his doctor.

In addition to cough and dyspnœa, there has been slight morning expectoration, occasional night sweats and possibly slight loss of weight. Sputum never noticeably offensive; no hæmoptysis at any time.

Past History.—Apart from the above symptoms, his health has been good, although he has been away from work owing to "bronchitis." Wound of right shoulder healed without any known complications. No symptoms at that time to suggest a wound of the lung.

Family History.—Father suffered from asthma. Wife attended Hospital on account of "chest trouble" in 1910. Three children alive and well.

Condition on Admission.—Marked clubbing of fingers. Temperature 97-99·8, pulse 70-90, respirations 24. General condition spare and muscular, skin sallow. Teeth carious, upper denture. Throat normal, tongue slightly coated. No glands palpable in neck. Urine normal. Cranial nerves and reflexes normal. Chest

[1] *Brit. Journ. Surg.*, 1927-28, xv, 334.

movements poor on both sides. Slight scoliosis of dorsal vertebræ to the right. Heart normal in size, position and sounds. Blood-pressure 145/80. Lungs (*see diagram*). Some restriction of movement of right side of chest, although both sides move poorly.

On percussion: impaired resonance from third rib to sixth on right side anteriorly and below the spine of scapula posteriorly. Over this area tactile fremitus is lost.

On auscultation: diminished air entry over area of impaired resonance. In latter position in front voice sounds are transmitted, but complete loss of voice conduction

FIG. 1.—X-ray after injection of lipiodol, showing tumour in right upper lobe.

behind. Over area mentioned, occasional coarse râles can be heard anteriorly, which clear after coughing. Abdomen, normal.

Sputum.—Mucopurulent, quantity about 1 oz. per diem; many pus cells; organisms very scanty, mostly small diplococci (like enterococci). *Bacillus tuberculosis* not found (two examinations).—Dr. N. Schuster.

Radiologist's Reports (Dr. P. Kerley, November 14, 1929).—Heart normal. Diaphragmatic movements slow on right side. There is a rounded shadow in the lower part of the right upper lobe, (?) neoplasm, (?) abscess.

November 28, 1929.—Appearances unchanged.

December 4, 1929 (examination after lipiodol injection, fig. 1).—Some of the lipiodol has entered the opacity normally; it may possibly be in front of the opacity which the oblique view has shown to be in the posterior part of the upper lobe.

December 11 (examination after induction of pneumothorax, fig. 2).—The right lung is evenly collapsed and the opacity is partly collapsed within the upper lobe.

Skiagram of hands shows a cyst in the head of the fourth right proximal phalanx.

Blood-count (Dr. Schuster).—Red cells 5,048,000, hæmoglobin 80%. White

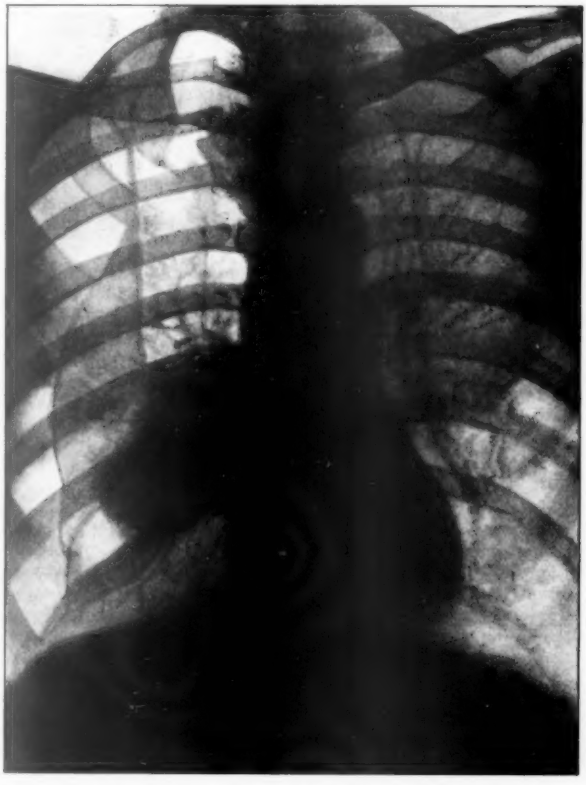


FIG. 2.—Showing tumour after induction of artificial pneumothorax.

cells 7,000 [*Differential:* Polymorphonuclears 4,600 (66%), lymphocytes 1,900 (27%), large mononuclears 420 (6%), basophils 70 (1%)].

Hydatid complement-fixation test negative. Wassermann reaction negative.

Thoracocentesis in the anterior and posterior axillary lines in the fourth and fifth spaces, and in the scapular line in eighth space, revealed no fluid in the pleura. The needle was also carried into the underlying lung without result.

The outstanding symptoms in this case are dyspnœa and cough, dating back to 1900, but worse during the last three months.

The physical signs are those of consolidated or compressed right lung in its middle zone. The skiagram shows a rounded mass in the lower and posterior portion of the right upper lobe. In one of the oblique pictures this mass appears to have a stalk.

Length of history, regular contour of shadow, and absence of wasting and of evidence of secondary deposits suggest that the mass is benign. Absence of pleural effusion is also against a diagnosis of malignant growth.

It is considered that the possibilities are either a chronic abscess of the lung or benign tumour either in the lung itself (e.g., a fibroma) or pressing on it from the mediastinum, in which case a dermoid cyst or teratoma must be considered.

Discussion.—Dr. H. V. MORLOCK said he thought the swelling was a chronic lung abscess. The patient looked ill and septic, and there was marked clubbing of the fingers, such as was particularly apt to occur in suppurating conditions of the chest. The man confessed to him that he had been ill only eleven months, and that he did not cease work until seven weeks ago. That favoured the idea of lung abscess. A benign growth alone would not give so much mucopurulent sputum. Moreover the skiagram showed an ill-defined outline except at its lower portion, which area corresponded to the interlobar fissure, and a benign growth would give a more definite one. He thought bronchoscopy should be carried out before finally deciding on the treatment.

Dr. R. E. SMITH said that the tumour might be a gumma, even though the Wassermann reaction was negative. He suggested giving iodide of potassium. Clubbing of the fingers also favoured syphilis.

Dr. PHILIP ELLMAN said that in view of the fact that the symptoms had become much more pronounced during the last three months the possibility of malignant degeneration of a benign tumour must be considered. Moreover a negative hydatid complement-fixation test did not necessarily exclude a hydatid cyst. He too considered it important that bronchoscopy should be done in this case.

A thoracotomy would of course clinch the diagnosis. An interesting feature in the case was the fact that an artificial pneumothorax had resulted from merely needling the chest in search for fluid.

The PRESIDENT asked whether Dr. Saxby Willis attached any importance to the absence of leucocytosis as a point against the diagnosis of abscess of the lung.

Dr. SAXBY WILLIS (in reply) said that chronic abscess was possible, but the absence of a leucocytosis in that event was unusual. Moderate leucocytosis had been present in every case of abscess of lung with which he had had to deal (ten during the last four years). The sputum was not so extremely offensive as was usual with abscess. Innocent tumours might certainly undergo malignant degeneration in later life as suggested by Dr. Ellman. Bronchoscopy had so far not been carried out because, judging from the appearance after lipiodol injection, he (the speaker) considered that the bronchus was free. As to gumma, he did not think it likely, but he agreed that one should not consider the negative Wassermann to be the final word; he would give a provocative injection of novarsenobillon, and would begin treatment with potassium iodide. He did not think the shadow had a sufficiently regular outline for the swelling to be a hydatid cyst. On the whole, he thought it most probable that the tumour was a teratoma.

POSTSCRIPT.—Bronchoscopy (Mr. A. M. Zamora) shows wall of right lower bronchus to be flattened slightly. No obstruction.

Section of Medicine.

[*January* 28, 1930.]

Nine Cases of Recovery from Diabetes Mellitus.

By O. Leyton, M.D.

In order that the title of this paper shall convey the same meaning to all, a definition of diabetes mellitus is essential. For the purpose of this paper the definition of diabetes mellitus is: "A disease due to a progressive deterioration of the metabolism, primarily of that of carbohydrate and secondarily of that of protein and fat." This deterioration may progress steadily, sporadically or fulminatingly; it may be arrested or even reversed by medical treatment. The diagnosis of diabetes has been based upon symptoms such as thirst, polyuria, dry tongue, lack of energy, loss of weight accompanied by a hyperglycæmia. I diagnose hyperglycæmic glycosuria in the absence of symptoms as diabetes mellitus only when there is conclusive evidence that the loss of power of storing sugar is progressive.

I regard a patient as having made a complete recovery when he has eaten ordinary food for at least six months and has at no time developed glycosuria. Naturally, during this period he has not received any drug calculated to assist metabolism nor to delay absorption. If the patient happens to have a low renal threshold for dextrose, the fact that the concentration of sugar in his blood has not risen above 0·19% after the principal meals replaced the absence of glycosuria.

Some of the cases have made only a partial recovery. I have assumed that the recovery is partial when the patient has been able to utilize a diet containing more carbohydrate than that which he received when he needed insulin. The diet must contain more than 90 grm. carbohydrate and at least 35 calories per kilogramme body weight per diem. There must have been a period of at least six months freedom from insulin.

About eight years ago Sir Archibald Garrod asked me whether I had ever seen a case of undoubted diabetes mellitus make a recovery; my reply was "never," and at that time I fear I should have received any story of recovery with an air of incredulity. That opinion is no doubt current to-day. If any holding that point of view happen to be present this afternoon, I would ask them to indicate any error in my diagnosis or to amend my conclusions on the question of recovery.

The nine cases I am about to record do not represent all in which hyperglycæmia has ceased to develop after meals, but since I do not admit that hyperglycæmic glycosuria is necessarily diabetes mellitus, only cases satisfying the definition are included. I have used the word "recovery" instead of the word "cure" in order to avoid making the assumption that the treatment has been responsible for the return to health. Since, however, the treatment to which these patients have been submitted is not that advocated by the majority of authorities on diabetes mellitus, a description of it may prove of interest. As more than six years have elapsed since I outlined this treatment, and as I have adhered to it during that time, perhaps you will forgive my repeating my former statements: "We have in insulin a substance which when injected into a diabetic, allows him to burn sugar. The question we have to consider to-day is how to use this substance to the greatest advantage of our patients. In order to answer that question I must remind you of the work done by F. M. Allen ten years ago. His experiments consisted in removing the greater part

of the pancreas and observing the condition which allowed life to be prolonged. The conclusion he arrived at was that overwork of the pancreas led to degeneration of that gland. This was an epoch-making discovery, the importance of which has not been fully appreciated, although it forms the basis of the successful treatment of diabetes mellitus. . . . Therefore if an attempt be made to arrest the disease in a diabetic, insulin must be given in sufficient quantity to prevent at any time a hyperglycæmia which will over-stimulate the β cells of the islands of Langerhans."

The mechanism through which the pancreas is stimulated has not been determined definitely, and this is not the time or the opportunity for me to lay before you the evidence in favour of a peripheral or central apparatus, but there is one thing upon which all are agreed, namely, that the concentration of sugar in the blood is the determining factor. The pancreas is stimulated into activity when the sugar in the blood rises above a certain concentration: in all probability this concentration not only differs in different individuals, but also varies from time to time in the same individual, but since I have not succeeded in discovering a method of determining this concentration in the diabetic subject, I have been arbitrary and have assumed it to be 0·15%. Although the treatment has been directed to keep the concentration of sugar in the blood below the figure in all cases treated, nevertheless in other respects the patients have been studied individually; the diets have not been fixed by reference to any tables which declare that a patient whose height is a certain fraction of a mile whilst his skin-surface is a certain fraction of an acre requires a certain number of calories in his daily food. I hold no brief for those who advocate a diet very poor in carbohydrates, or for those who assert that so long as the quantity of fat is kept low the patient may receive plenty of carbohydrate. In my experience some patients are able to take more carbohydrate than fat, but this is far from the general rule, except amongst the obese. All my patients have received sufficient food to satisfy their appetites and the majority sufficient to allow them to gain or maintain their weight. A few have been obese and their diets have been arranged for them to lose weight. None of the nine patients has received alcohol. The views on the advisability of administering alcohol to diabetic patients have changed from time to time. Fourteen years ago it was given in comparatively large quantities because it was thought to be able to supply energy in a form which could be used. Later, several observers, myself among them, found that on ceasing to give alcohol, the weight of the patient did not fall and that there was no evidence that it served any useful purpose. I think that during the last few years evidence has been accumulating to prove that it retards regeneration of the pancreas and acts as a poison in a way comparable with chloroform and ether, but in a degree less potent.

There has not been any fixed interval between the injections of insulin and the meal; the time has differed in different patients from five to ninety minutes, depending entirely upon the concentration of sugar in the blood before and after meals. The number of meals and the hours have been arranged to suit the individual patient. Frequently it has been found necessary for carbohydrate to be taken at 11 a.m. and 10 p.m. in order to prevent the development of hypoglycæmic attacks towards midday and midnight. In cases in which attempts were made to prevent these attacks by decreasing the dose of insulin, the concentration of sugar in the blood rose to over 0·15% about an hour after the meal. I am not satisfied that a patient under my care is being treated correctly until it has been proved that the concentration of sugar in the blood at all times during the day and the night does not rise above 0·15%; one can be certain of this only by taking samples of blood and estimating the sugar in them. After the correct diet and dose of insulin have been established, further observations become necessary when any reduction is made in the dose of insulin.

The difference between the treatment I have adopted and that advocated by the majority may be summed up in the following words: Most advise the administration

of the minimum dose of insulin which will render the patient free from glycosuria whilst on a fixed diet; I give the maximum dose of insulin which the patient can stand whilst on a fixed diet. It may be alleged that the nine cases of recovery which I produce represent an extremely small percentage of those which have been under my care, and that these cases would have recovered with any alternative treatment. If, however, observers with an equal experience of diabetes mellitus have failed to attain positive results with cases treated in the more orthodox manner, I am forced to the conclusion that the method I have adopted has been instrumental in promoting recovery.

I attribute the small percentage of recoveries to a variety of causes; amongst them are:—

(1) The fact that patients are not treated with insulin immediately upon the development of the disease; the longer the interval between the onset of the disease and the commencement of the above treatment, the more remote the chance of making a complete recovery. Until the world sees a new generation of medical practitioners it will not become the general rule to treat diabetes mellitus with insulin from the onset of the disease. There are few things more dramatic in medicine than the improvement, unfortunately only temporary, which follows upon the restriction of diet, in any patient suffering from diabetes mellitus. Those who have seen this remarkable change in their patients will be persuaded only with difficulty that any better treatment is a practical policy. There is also a prevalent belief that once a patient is started on a course of insulin, he must continue that treatment for the rest of his days. The practitioner therefore postpones the use of insulin until the life of the patient is threatened, which usually is at a point long past the period when complete recovery is possible.

(2) The second factor inimical to recovery is infection. A patient who appears to be making good progress, to such an extent that it has been necessary to reduce his dose of insulin on several occasions, suddenly experiences thirst, polyuria and glycosuria. In other words, he has a second attack of the disease, or has developed some acute infection which may in many ways simulate a second attack. The differential diagnosis between the two conditions must depend upon the discovery of the source of infection. If no source can be discovered it is assumed to be a second attack. At the same time it should be observed that whilst infections are common, second attacks are rare. The return to the condition which prevailed before an infection is often fairly rapid, but after a second attack the progress is tediously slow. A considerable number of budding recoveries have been nipped by infections in a most disheartening manner.

(3) The third factor is the difficulty of adhering to the rule that the concentration of sugar in the blood must never rise above 0·15%.

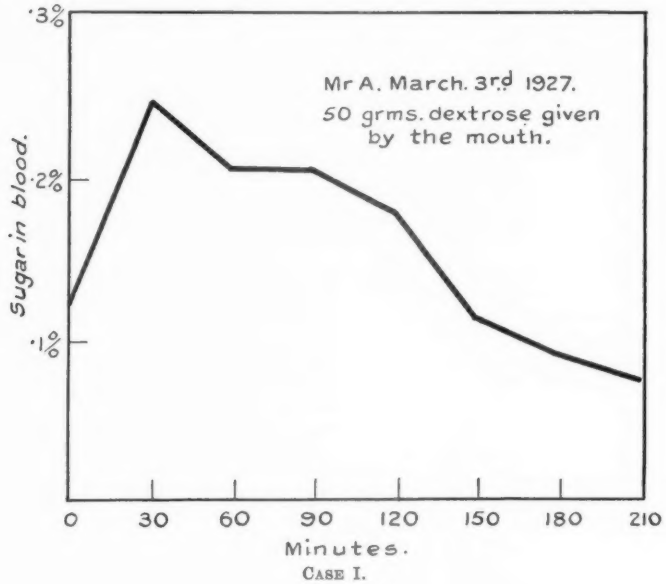
My cases of recovery have been confined (with one exception which is not included in to-day's list) to private patients. It is essential that the patient should be intelligent and scrupulously obedient. Even then there are difficulties. The concentration of sugar in the blood tends to rise during the night, and in some cases is well above the limit by six o'clock in the morning unless a dose of insulin be given about one a.m. This is extremely inconvenient. The promise that a recovery would result from following the prescription for a year would no doubt remove all objections, but only quacks guarantee recoveries; therefore the number of patients willing to have this injection has been comparatively small. By the use of insulin suspended in castor oil injected towards six o'clock in the evening, I believe that this difficulty of the rise of sugar in the blood during the night will be overcome. The absorption of insulin in oil is slow and the action prolonged.

My object in bringing the cases before you is to invite criticism. Should any speaker take the view that these cases are not due to subinsulinism but to hyperpituitarism, I trust that he will favour us with detailed reasons for that conclusion.

Case I.—Mr. A., aged 66. First seen October 16, 1924.

Family History.—None of diabetes mellitus.

Fourteen days previously he had had a cold, and ten days ago his mouth became dry, even shortly after taking fluid. He suffered from intense polyuria, having to pass urine at intervals of less than an hour, and he noticed it was practically colourless. Nine days later he began to feel really ill. I found that his urine contained much sugar and that the concentration of sugar in his blood at 12.50 (four hours after a meal) was 0·31%. He came under treatment immediately, and upon a limited diet containing about 70 grm. of carbohydrate, it needed 10 units of insulin injected twice a day to keep the concentration of sugar in the blood under 0·15%. From time to time samples of blood were taken in order to be certain that this figure was not exceeded. In March, 1925, after a luncheon containing 30 grm. of carbohydrate, the sugar in his blood rose to 0·19%, and therefore he was told that he could not take as much as this at a meal without having insulin previously. He



Case I.

was quite willing to reduce the diet. Estimation of the concentration of sugar in his blood was made at intervals of a week for some time, and on no occasion was it found to rise above 0·15%.

On March 3, 1927, after 50 grm. of dextrose by the mouth, the sugar in his blood rose to 0·25%; it fell again to 0·107% within 120 minutes. His diet was gradually increased.

On February 13, 1929, at 5 p.m., the concentration of sugar in his blood was 0·14%. On being asked whether he had now returned to a perfectly normal diet he replied, "I do not take sugar with apple tart." In January, 1930, he reported "all well," and sugar in blood was 0·14%.

Analysing this case, there seems to be little doubt that the patient had true diabetes mellitus, for he had thirst, polyuria, glycosuria and hyperglycæmia even

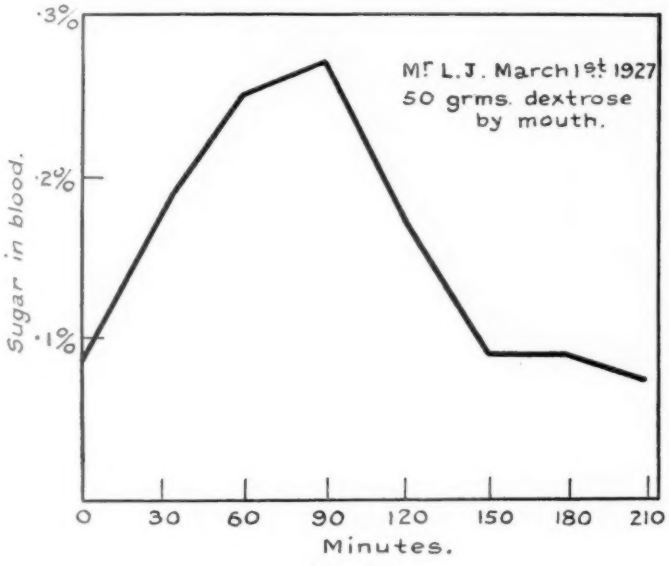
four hours after a meal. There can be little doubt about his recovery. In February, 1929, whilst he was on a perfectly ordinary diet including bread, potatoes and puddings, the sugar in his blood was 0·14%, and he described his health as perfect.

Case II.—Mr. L. J., aged 49. First seen March 1, 1926.

Family History.—None of diabetes mellitus.

Whilst in Torquay on holiday he suddenly developed severe thirst, and on consulting a doctor was told that he had sugar in his urine and should seek advice in London without delay. At 12.10 p.m. the sugar in his blood was 0·30%. He was placed in a nursing home and given a restricted diet containing 70 grm. of carbohydrate. On March 3 the sugar in his blood was: at 7.45 a.m., 0·23%; 9 a.m., 0·33%; 2 p.m., 0·20%; 6.30 p.m., 0·23%; 10·30 p.m., 0·27%.

The dose of insulin was gradually increased to 20 units twice a day, and on March 11 the sugar in his blood was: at 7.30 a.m., 0·13%; 9 a.m., 0·13%; 12.30 p.m., 0·11%; 6.35 p.m., 0·11%; 8.15 p.m., 0·11%.



CASE II.

On April 12, at 11.40, the sugar in his blood was 0·10%, and the insulin was reduced to 15 units twice a day. On May 17 the dose of insulin was reduced to 12½ units and 10 units because the patient had been suffering from hypoglycæmic symptoms. The sugar in his blood at mid-day was 0·07%. On July 1 the sugar in his blood towards mid-day was 0·115%, the insulin having been reduced to 10 and 8 units because he had had severe attacks of hypoglycæmia. On August 6 a further reduction to 7 and 6 units, the blood taken at 4.30 containing 0·12%.

The blood taken in September, October and December was all within the limits of normal, and the dose of insulin was reduced to 10 units once a day. On this dose he continued until March 1, 1927, when an hour after breakfast the sugar in his blood was 0·09%. He was then submitted to a tolerance test, 50 grm. of dextrose

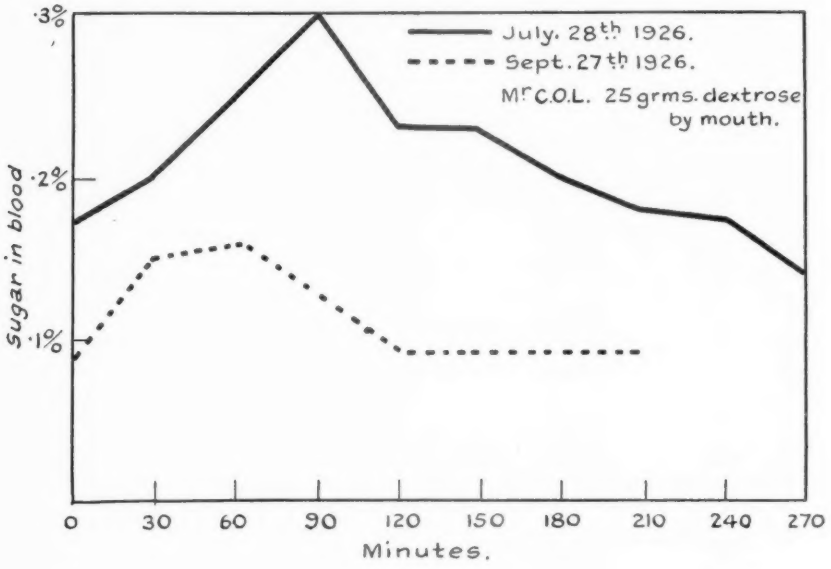
being given; he was able to store carbohydrate at the rate of 33 grm. per hour, which is roughly about half the average efficiency. He ceased taking insulin.

On November 16, 1927, the sugar in his blood at mid-day was 0·12%, at 2.45 0·11%. On January 1, 1928, at 5 p.m. it was 0·13%. In April, 1929, he had rather severe bronchitis, but the sugar in his blood shortly after mid-day was 0·08%. The patient found that his diet, which was only slightly restricted, satisfied him completely, and he was not willing to add to it in any respect.

Analysis.—The sudden onset of the disease with intense thirst and hyperglycæmia left no reasonable doubt that it was one of true diabetes mellitus. The evidence of the hyperglycæmia did not rest upon a single observation but upon a series of observations. That the recovery was fairly complete is proved by the fact that he was able to store or burn 33 grm. carbohydrate per hour; that it was permanent was shown by the observation that in April, 1929, the sugar in his blood was normal whilst he had not received insulin since March 1, 1927.

Case III.—Mr. C. O. L. First seen July 27, 1926, aged 47.

Family History.—Mother diabetic, two brothers refused life insurance due to glycosuria.



CASE III.

Came home from holiday in France because he had developed breathlessness and intense thirst along with some changes in his vision. These changes in refraction were stated by Mr. Flemming to be typical of diabetes mellitus. When he came to see me he had been on a carbohydrate-free diet, and at 3.40 p.m. the concentration of sugar in his blood was 0·16%, so that obviously he had reacted well to the restricted diet. With the history he gave me it seemed unwise to advise him to go on with an ordinary diet before submitting him to a carbohydrate metabolism efficiency test. He was told to present himself the following morning having had only a cup

of tea for breakfast. The sugar in his blood was 0·17%, and therefore he was given a small dose of only 25 grm. of dextrose by the mouth dissolved in 200 c.c. of water to which a little acid had been added. The concentration of sugar in his blood rose to 0·3% and had not fallen to 0·17% after 160 minutes. The patient was placed upon a restricted diet and 10 units of insulin twice a day.

On September 24 he decided to come under close observation, but the sugar in his blood was found to be as low as 0·06%. On September 27 he was submitted to a similar test to that which had been carried out at the end of July, and then the sugar in his blood rose to 0·16% and took only eighty minutes to fall to 0·09%. On September 29 he was given 50 grm. of carbohydrate and the sugar in his blood rose to 0·21%. He was advised to keep on a limited diet, and until November 19 took only 23 calories per kilogram of body weight per diem. Since he lost weight his diet was then raised to 30 calories per kilogram bodyweight.

On January 14, 1927, he was given 50 grm. of dextrose. It was then found that sugar in his blood did not rise above 0·12% and fell to 0·08%, and that therefore his power of utilizing sugar was up to the normal, and he was advised that he could eat and drink whatever he liked. In April, 1927, the concentration of sugar in his blood was satisfactory, and therefore I suggested that for a short time he should do himself very well indeed in order that we might find out whether his metabolism could stand up against a big strain. On May 13, 1927, the concentration of sugar in his blood after lunch rose to 0·22%, which led to the advice that it would be wise for him to eat only as much as was necessary to satisfy his hunger. Since that time he has presented himself at intervals, and I have failed to find any hyperglycæmia on any occasion.

Analysis.—The diagnosis in this case was based upon intense thirst, glycosuria, and changes in the refraction of the eyes. I gathered that the doctor in France was of the opinion that the breathlessness was air hunger, but of course of this I have no evidence. The sugar in his blood, following a comparatively small dose of dextrose, rose to 0·3% and took a long time to fall, and therefore I think one is justified in concluding that this is a case of diabetes mellitus. About his return to health there can be no doubt.

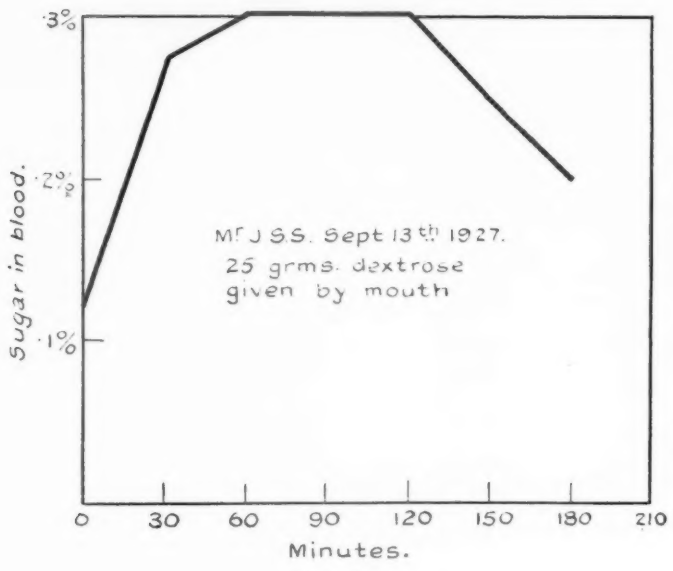
Case IV.—Mr. J. S. S., first seen September 12, 1927, aged 54.

Family History.—Some diabetes.

Recently developed severe thirst; sugar in blood at mid-day was 0·33%. After fourteen hours' fast the sugar in his blood on September 13 was 0·12%. 25 grm. of dextrose was given by the mouth, and the sugar in his blood was found to be at 10.5 a.m. 0·27%, 10.35 a.m. 0·30%, 11.5 a.m. 0·30%, 11.35 am. 0·30%, 12.5 p.m. 0·25%, 12.35 p.m. 0·20%. During this time 274 c.c. of urine was passed containing 4·6% sugar and 1·6% urea.

He was placed upon diet and increasing doses of insulin. On September 27 when receiving 15 units twice a day the sugar in his blood was at 9.35 a.m. 0·11%, 1 p.m. 0·10%, 2.15 p.m. 10%, 4.45 p.m. 0·143%. He kept to his diet and insulin, and from time to time the sugar in his blood was estimated. On November 29, 1927, the sugar in his blood was: at 9.30 a.m. 0·107%, 12.5 p.m. 0·10%, 1.15 p.m. 0·14%, 5 p.m. 0·10%. He said he had not felt better in his life. No hypoglycæmic symptoms.

On February 8, 1928, hypoglycæmic symptoms began to appear, and in order to appease them he added some carbohydrate to his diet. In April, 1928, the sugar in his blood at 5 p.m. was 0·09%, and the insulin was reduced to 12½ units twice a day. On November 30, 1928, the symptoms of hypoglycæmia led to the reduction of insulin to 7½ units twice a day and later to 5 units twice a day. In March, 1929, on 5 units twice a day, the sugar in the blood was: at 9.30 a.m. 0·107%, 2 p.m. 0·125%, 5 p.m., 0·09%. The carbohydrate in the diet had been added to, to a small extent.



CASE IV.

On March 20, after insulin had been omitted in the morning for a week, the sugar in his blood was: at 9.30 a.m., 0·15%; 2 p.m., 0·14%; 5 p.m., 0·10%. Insulin was stopped, and after four days the sugar in the blood was found to be: at 9.30 a.m., 0·14%; 2 p.m., 0·14%; 4.50 p.m., 0·10%.

November, 1929.—Patient reported progress. Felt quite well. Concentration of sugar in blood at 2.5 p.m., 0·09%.

Case V.—Major E., aged 40. First observed, September, 1927.

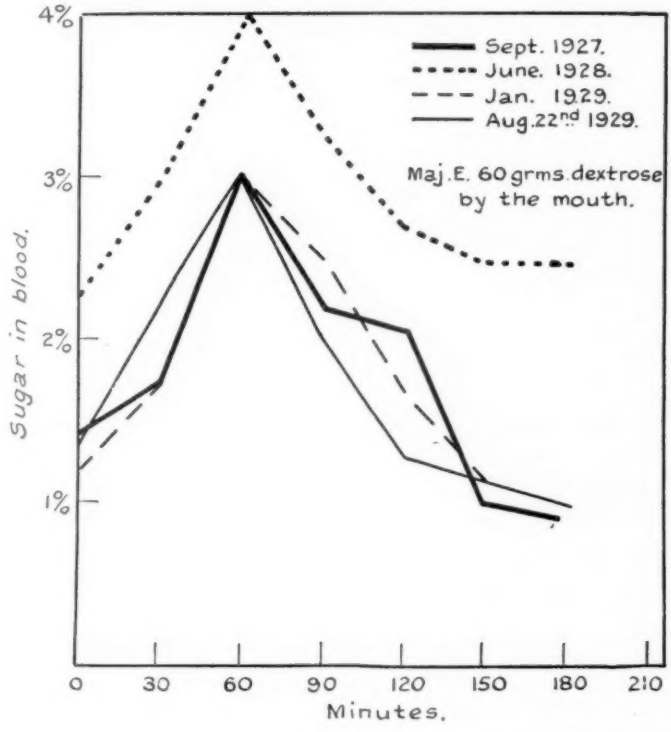
Family History.—None of diabetes mellitus.

This patient sought advice because he had been rejected for life insurance and upon making inquiries had learnt that his urine contained sugar. Some weeks previously he had been operated upon for hæmorrhoids. He had been taking an ordinary diet fairly rich in carbohydrate, and on September 19, 1927, after fourteen hours' fast the sugar in his blood was 0·14%. He was given 60 grm. of dextrose and his blood was examined at half-hourly intervals and found as follows: 0·175%, 0·30%, 0·22%, 0·21%, 0·10%, 0·09%. All the specimens of urine passed at these various times contained either a considerable quantity or a trace of sugar, so that there seemed to be evidence that the renal threshold was below the average. Since the patient had been subjected to an operation and an anæsthetic comparatively recently, I thought that this curve did not necessarily indicate diabetes mellitus, and I advised him to take a holiday for six weeks and then be submitted to a similar test. The patient had no symptoms of diabetes mellitus and not very long previously had passed a full Army test. His weight had remained constant during the previous four years.

Instead of returning after six weeks the patient presented himself on June 11, 1928, and then stated that, with the exception of occasional cramp in the legs, he was enjoying perfect health. He had no thirst and no polyuria. After fourteen hours' fast the sugar in his blood was 0·23% and at half-hourly intervals following the administration of 60 grm. of dextrose was: 0·3%, 0·40%, 0·33%, 0·27%, 0·25%,

0·25%, whilst the urine passed during this time contained 3% of sugar. This test seemed to be good evidence that the patient had developed diabetes mellitus.

The next step taken was to see whether he reacted to insulin. On June 19, whilst on diet, the sugar in his blood at 10 a.m. was found to be 0·17%, at 12.30 0·26%, and at 2.30 0·23%. This confirmed the earlier readings following the administration of dextrose. On a diet of 78 grm. of carbohydrate and 10 units of insulin twice daily the sugar in his blood was kept below 0·15% at all times, and he continued this dose until September 3, when it was found that the dose of insulin could be reduced to 5 units twice a day.



CASE V.

In January, 1929, he was subjected once more to a test with 60 grm. of dextrose by the mouth after he had rested from insulin for one week. The sugar in the blood recorded was: 0·125%, 0·18%, 0·30%, 0·25%, 0·17%, 0·12%, 0·10%, showing that he had returned to the state that he was in when he first came in September, 1927. Insulin was then resumed because, obviously, complete recovery had not occurred.

In August, 1929, he passed through the test of 60 grm. of dextrose for the third time, and during that test the sugar in the urine was only 0·5%, whilst the sugar in the blood rose to 0·30% but fell more rapidly than on the previous occasion. He was

advised to continue a restricted diet until the beginning of November and then to eat and drink what he liked. On November 11, 1929, the sugar in his blood an hour after breakfast was 0·15%; an hour after lunch 0·16%, and an hour after tea 0·107%. I conclude, therefore, that this patient's condition has ameliorated greatly.

It is too early to state whether it is a complete recovery, because it is only after a patient has thrown work upon his pancreas for many months without the pancreas showing any signs of degeneration that one may conclude that recovery has occurred.

Case VI.—Captain R. H. P. First seen November 6, 1927, aged 34.

Family History.—None of diabetes mellitus.

Gave a history that in March, 1927, whilst on a shooting trip in Khartoum suffered from malaria. Felt ill in July and developed severe thirst along with dryness of mouth in August. Noticed that he was losing weight in September, and by November 26 he had lost 3 st. Along with the usual symptoms of diabetes mellitus he had constipation and cramp in his leg. At mid-day on November 26, 1927, the sugar in his blood was 0·30%. He was placed in a nursing home, given a fixed diet and an increasing dose of insulin. On 25 units twice a day the sugar in his blood on December 13 was: at 9.40 a.m. 0·12%, 12 noon 0·06%, 2.30 p.m. 0·13%, 5.20 p.m. 0·09%, 8.30 p.m. 0·08%.

In December, 1927, he went to Switzerland and took sun baths, and whilst in Switzerland he began to have hypoglycæmic attacks and reduced his insulin. On January 30, 1928, the insulin was reduced to 13 units and 10 units, and upon this the sugar in his blood was: at 11 a.m. 0·17%, 2.40 p.m. 0·107%, 5.20 p.m. 0·12%. On January 31 the test was repeated, and at 11 a.m. the sugar in his blood was found to be 0·19%, and therefore insulin was raised to 15 units twice a day. On March 5 the sugar in his blood was: at 10 a.m. 0·11%, 12.43 p.m. 0·125%, 2.45 p.m. 0·16%, 4.45 p.m. 0·13%. He confessed to having taken half a roll at his lunch, which accounted for the sugar in his blood being 0·16% at 2.45 p.m. The insulin was reduced to 10 units twice a day. On April 11 the sugar in his blood was: at 9.45 a.m. 0·13%, 12.40 p.m. 0·107%, 2.45 p.m. 0·13%, 5.20 p.m. 0·13%. I advised a reduction to 8 units twice a day. In May severe tonsillitis developed; he was removed to a nursing home, the fat in his diet was cut down, and it was found necessary to increase the dose of insulin to 25 units twice a day to reduce the sugar in his blood to normal limits. On June 18, 1928, the insulin was reduced to 12½ units twice a day because he had had a severe hypoglycæmic attack. The sugar in the blood was at 10 a.m. 0·1%, 12.20 p.m. 0·08%, 2.35 p.m. 0·15%, 5 p.m. 0·12%. A week later observations were made to see whether this reduction in insulin was justifiable, and the sugar in the blood was: at 10 a.m. 0·09%, 12.20 p.m. 0·09%, 2.30 p.m. 0·08%, 5 p.m. 0·09%. The insulin was then reduced to 10 units twice a day. On August 22 the sugar in the blood was: at 10 a.m. 0·11%, 1 p.m. 0·11%, 2.35 p.m. 0·125%, 5 p.m. 0·12%, and the insulin was reduced to 6 units twice a day. On September 18 the sugar in the blood was at 10 a.m. 0·09%, 1 p.m. 0·09%, 2.35 p.m. 0·14%, 5 p.m. 0·13%. The insulin was reduced to 5 units twice a day, and he was advised to cease taking insulin fourteen days before the next visit. On November 30, 1928, the sugar in the blood after ceasing insulin for fourteen days was: At 10 a.m. 0·09%, 12.30 p.m. 0·09%, 2.40 p.m. 0·075%, 4.45 p.m. 0·11%. In January the sugar in the blood was found to be normal. During that month the patient had influenza, but it did not affect the sugar in his blood. He was advised to increase his diet to 25 grm. of carbohydrate at each of the three meals. On August 29, 1929, he was submitted to a sugar tolerance test, but he had a boil in his ear at that time and it was found that the sugar in his blood after fourteen hours' fast was 0·20%. It rose to 0·60% and fell to 0·37% three hours after the administration of the dextrose. His urine contained 2·5% of sugar. He was advised to go back on to insulin until the boil in his ear had healed. On September 19, after having ceased to take insulin for a fortnight, the sugar in his blood at 2.45 p.m. was 0·12% and at

4.30 p.m. was 0·15%. On November 21, 1929, the sugar in his blood was at 10.20 a.m. 0·16%, 12.35 p.m. 0·17%, 2.40 p.m. 0·14%, 5.20 p.m 0·19%.

Analysis.—The evidence that the patient was suffering from diabetes mellitus is quite unquestionable. One cannot consider that the recovery is complete because his metabolism still remains very sensitive to bacterial toxins, but it seems probable that as time passes his pancreas will become more and more efficient.

Case VII.—C. B., male, aged 5, December 21, 1927. Family history of diabetes mellitus. Elder brother died from that disease. When first seen the patient was very drowsy, had a raised temperature, sugar in the urine and complained of pain in the upper part of the abdomen. The concentration of sugar in the blood was 0·25% several hours after food. Patient was placed upon a diet: carbohydrate 80 grm., protein 85 grm., fat 85 grm., and needed 7½ units insulin twice a day to keep the sugar in his blood below 0·15%. As time passed hypoglycæmic symptoms developed, and in the following March insulin was stopped. The diet was increased to C. 95, P. 85, F. 85. May 24, 1928.—Following a rat bite the temperature rose and glycosuria reappeared and the patient needed 3 units of insulin twice daily to control the sugar in the blood. During the following month the patient developed a common cold and gradually the dose of insulin had to be increased, until in October he was receiving 15 units daily. In January, 1929, owing to another cold, the insulin had to be increased to 17 units daily. Further infections needed further increases in the doses of insulin, and by February 8 the patient was receiving 18 units of insulin twice a day, i.e., 36 units daily. Recovery from the cold was rapid and was accompanied by the development of hypoglycæmic symptoms.

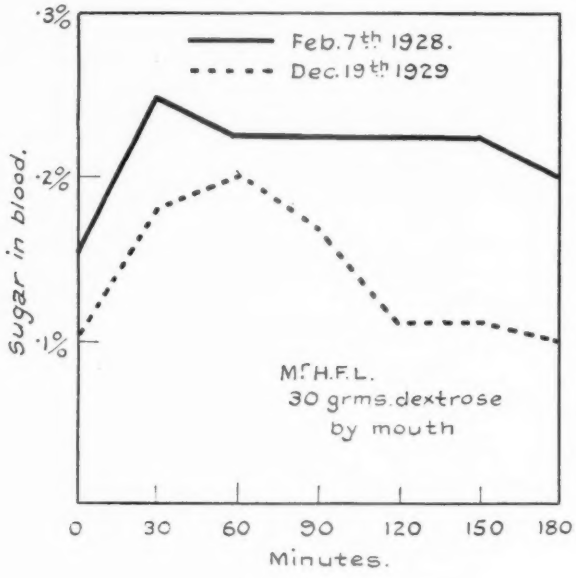
February 12.—The dose of insulin was reduced to 10 units twice a day. By February 17 the dose had come down to 6 units twice daily. On that day however only the morning dose was given because hypoglycæmic symptoms developed after the mid-day meal. The patient then went through a period of persistent hypoglycæmia which called for vigorous treatment with carbohydrate at two-hourly intervals for a time, and for weeks the patient was awakened during the night in order that he might be given sugar. March 24, 1929.—The diet had been increased to C. 155 grm.; P. 67 grm.; F. 77 grm. The concentration of sugar in the blood was at 8 a.m., 0·05%; 10.30 a.m., 0·08%; 1.15 p.m., 0·08%; 2.30 p.m., 0·17%; 4 p.m., 0·10%; 7 p.m., 0·14%. March 25, 1929.—1 a.m., 0·10%; 5 a.m., 0·11%. April 28, 1928.—Diet: C. 165, P. 62, F. 74: 10.45 a.m., 0·075%; 1 p.m., 0·10%; 3 p.m., 0·12%; 5 p.m., 0·17%; 6 p.m., 0·13%; 7 p.m., 0·12%; 9.0 p.m., 0·14%; 10.45 p.m., 0·20%. April 29.—3 a.m., 0·10%; 7 a.m., 0·08%. Since the sugar in the blood rose above 0·15% for a period, the diet was reduced somewhat. Observations have been continued up to December 12, 1929. Since the patient was very susceptible to the common cold it was thought advisable to give him a vaccine. It was found that the bacterial poison drove up the concentration of sugar in the blood to 0·20%, but it did not remain there for long. This hyperglycæmia following the introduction of bacterial poison is the reverse to what happens in a normal individual and seems to indicate that there is some disease of the metabolism. In this case the disease must be very mild indeed. The patient keeps a concentration of sugar in the blood within the limits of normal whilst on a diet containing over 50 calories per kilogramme body weight per diem and more than 90 grm. of carbohydrate, nine months after he has ceased to receive insulin.

Case VIII.—Mr. H. F. L. First seen February 6, 1928. Aged 54.

Family History.—Mother diabetic, brother diabetic, two other brothers refused life insurance owing to glycosuria.

This individual had previously insured his life at a normal rate. He found that he was losing weight and felt ill, and upon consulting his doctor sugar was found in his urine. His gums were severely infected. At 5 p.m. the concentration of sugar

in his blood was 0·21%. On February 7, in the morning, after fourteen hours' fast, the sugar in his blood was 0·15%. He was given 30 grm. of dextrose, which led to the sugar in his blood rising to 0·25% and taking three hours for it to fall to 0·15%. He was given 10 units of insulin along with a limited diet, and this was found to keep the sugar in his blood below 0·15%. Insulin was stopped on May 19, and on May 21 the sugar in his blood was found to be normal. On June 5 he was given



CASE VIII.

40 grm. of dextrose, that is 33% more than at his original test in February, and the sugar concentration in his blood rose to 0·16%. He was advised to keep the carbohydrate in each meal under 30 grm., otherwise the diet was not restricted.

Case IX.—Miss M. J., aged 65. August 16, 1928. Severe thirst for three months, which had become still more accentuated during the last few weeks. She complained of pains in the legs and loss of energy. Four hours after food, at 12.30 p.m., the concentration of sugar in her blood was 0·31%. The weight of the patient was close upon 17 st., and therefore she was put upon a diet which contained only a little fat, 70 grm. carbohydrate and 100 grm. of protein. It was found that 15 units of insulin twice a day kept the sugar in her blood below 0·15%. August 24, 1928, the sugar in the blood at 9.40 a.m. was 0·13%, 12 mid-day 0·08%, 9.30 p.m. 0·07%. November 8, 1928: Weight had fallen to 16 st. The patient had been suffering from mild hypoglycæmic attacks. The concentration of sugar in her blood at 12.50 p.m. was 0·09%. The dose of insulin was reduced to 10 units twice a day. February 7, 1929: Weight had fallen to 15 st. 7½ lb. A history of further hypoglycæmic attacks led to the reduction of dose of insulin to 8 units twice a day. March 18, 1929: Concentration of sugar in the blood: at 11 a.m. 0·13%, 12.30 p.m. 0·10%, 2.30 p.m. 0·14%, 4.30 p.m. 0·125%. Insulin dose reduced to 5 units twice a day. May 7, 1929: Concentration of sugar in the blood: 10.45 a.m. 0·14% (biscuit eaten

at 11.0 a.m.), 12.30 p.m. 0·14%, 2.30 p.m. 0·12%. Advice was given to cease taking insulin. December 10, 1929: Concentration of sugar in the blood: 11 a.m. 0·125%, 12.40 p.m. 0·09%, 2.20 p.m. 0·115%, 4.30 p.m. 0·107%. This case seems to conform to the usual onset of diabetes mellitus. The recovery in December was only partial; the sugar in the blood of the patient was low, whilst insulin had been stopped more than six months before the observations were made. The diet of this patient has been increased.

Dr. Leyton's paper was criticized at some length by Dr. Cammidge, Dr. George Graham, and Dr. R. D. Lawrence, who joined in disputing the justice of the term "recovery" as used by Dr. Leyton, and regarded the state of improvement recorded as by no means so uncommon as Dr. Leyton had assumed, Dr. Poulton also discussed the paper and Dr. Leyton replied.

Psittacosis: A Further Account of Cases of Human Infection,

By A. P. Thomson, M.C., M.D.

With Bacteriological Reports

By W. T. Hillier, M.R.C.S., L.R.C.P.

In a recent communication [1] I published a brief review of psittacosis and described four cases of human infection that had come to my notice. My reason for returning so soon to the subject is that I have since met with no less than thirteen further cases, which are recorded fully below.

One of them (Case 11) I did not myself see, but the clinical details leave no doubt of the diagnosis; of the remaining twelve, two instances (Cases 6 and 7) were not sufficiently clear cut to warrant a final opinion, but I regard them as probable instances of mild infection.

The fact that so many cases, in so short a time, have come to the notice of one physician seems to justify the tentative opinion that I expressed previously that sickness of this type is by no means rare. It is true that in Cases 5, 6 and 7, I was consulted as a result of the publicity given to my first communication by a daily newspaper, but most of the others occurred in the ordinary course of practice, and I saw them as unsolved problems of obscure pyrexia: in several instances a fairly confident diagnosis was made on purely clinical grounds, for the history of contact with sick birds was only elicited later, and although one (Case 8) occurred in a doctor's household, the possible significance of this point had not previously been suspected.

Cases 5, 6 and 7.—For information and help in preparing the record of the following cases I am indebted to Dr. W. Geoffrey Shaw, of Weaverham, Cheshire, who had charge of them, and to Dr. W. H. Grace, Pathologist to the Royal Infirmary, Chester, who saw them in consultation.

On June 27, 1929, Mrs. A. bought a young parrot from a dealer in London. The day after its arrival in her home the bird appeared to have a "cold": a little later the feathers became ruffled and were shed freely, and there was a frothy discharge from the nose; diarrhœa set in on July 20, and on the 22nd the parrot died. The bird had been much petted by Mr. A., who trained it to walk up his arm and take a lump of sugar from between his lips, and his little son had often played with it. Mrs. A. cared for it during the later stages of its illness. On the day that the parrot died, Mr. A. (Case 5), who had appeared unwell for two days previously,

collapsed at his work, and on returning home was found to have a temperature of 103° F. As Dr. Shaw could find nothing to account for the fever, he invited Dr. Grace to see the patient the following day, and the latter has kindly sent me the following report:—

"When I first saw him, he had a distinctly high temperature and felt ill. Clinically, to me, he did not quite fit in with a case of typhoid, or paratyphoid; the onset was rather sudden—although I tried to persuade myself that he had been walking about for some time with a pyrexia and had refused to give in—and he seemed to be more suddenly ill than one usually finds in one of the typhoid group infections. When I saw him he was almost on a point of a rigor; his conjunctivæ were very injected, and he was more brightly spoken than one usually sees in a case of typhoid or paratyphoid infection. I could not see any spots, nor could I feel his spleen, nor could I find anything abnormal in the chest. I took some of his blood, and with the Medical Research Standard Agglutinable Emulsions I did his serum against typhoid and paratyphoid A and B. To my surprise he gave quite a quick and complete agglutination of the *B. typhosus* up to 1 : 300 and a slight agglutination of the *B. paratyphosus* A and B to 1 : 10. With these results I was prepared to throw overboard my clinical impressions and, for the moment, call it a case of pure typhoid and advise them to treat it accordingly. I have since examined fæces, urine, blood, parrot's perch and scrapings from the bottom of the parrot's cage, but in no case have I found a non-lactose-fermenter."

Mrs. A. from the very beginning of her husband's illness had insisted that he had been infected from the parrot, and searched any literature that she could find bearing on diseases of birds that might be transmitted to men; she had no success, however, until she came across a paragraph in the newspaper referring to my first paper in the *Lancet*, which she immediately obtained.

In these circumstances I saw Mr. A. in consultation with Dr. Shaw on July 28. For the previous six days his temperature had been constantly high, between 103° F. and 104° F., but his pulse had remained slow—it never reached 100 per minute and was usually between 80 and 90. He was flushed and sweating profusely, and complained of intense headache: he was mentally clear, but at times he had been mildly delirious. An irritable cough had developed two days previously, and as I entered his room he expectorated some rusty sputum, but this never recurred.

On examination I found, at the right base in the axillary line some fine crepitant râles and a patch of rather doubtful faint tubular breath sounds. Dr. Shaw and I agreed that at that stage he looked rather like a case of pneumonia. There was no serious abdominal distension: the spleen was not palpable, there were no typhoid spots—merely a few sudamina. The bowels were costive. A blood-culture I made at the time proved sterile (as did Dr. Grace's), and I recovered nothing of significance from a postnasal swab. The piece of rusty sputum that I took away with me yielded a Gram-negative non-lactose fermenting bacillus, but I was never able to get it in pure culture, and eventually it died out. Later Dr. Shaw sent me the following report on the progress of this case: "As far as the clinical aspect is concerned, he appeared to be a typical typhoid. The temperature curve reached its maximum at the beginning of the second week, then remained at a steady 100° F. to 101° F., and in the third week came down by lysis. During the whole febrile period he complained of intense headache and had troublesome cough, with scanty muco-purulent sputum. The tongue was thickly furred and the bowels were obstinately constipated throughout. The small spot in the right lung, where you suspected a commencing broncho-pneumonia, did not extend, and there were no further pneumonic signs. The pulse remained slow (about 80 to 85) and of good tension throughout the illness. His convalescence was uneventful."

Two or three days before Mr. A. became seriously ill, his son (Case 6), aged 7 years, fell sick with an acute febrile attack (on one occasion the mother found a temperature of 103° F.). After four or five days the temperature became normal, but

continued to go up to 99° F. each evening for a fortnight. During that fortnight he always declared that he felt perfectly well, and he certainly had no symptoms of any kind except constipation, but looked rather pale and washed out. I examined this boy with Dr. Shaw on July 28 and agreed with him that there were no abnormal physical signs. It is probable that this child was infected from the bird with which he had been in close contact, for he became ill at about the same time as his father, and it is well known that in children infections of the typhoid group run a much milder course than they do in the adult.

Mrs. A. (Case 7) had a remarkable experience. On July 25, when her husband had been in bed for three days, she complained of backache and of feeling ill. On the following day, in view of Mr. A.'s positive Widal, she was given a protective dose of T.A.B. vaccine (500 millions of *B. typhosus* and 250 millions each of paratyphosus A and B). One and a half hours after the inoculation she had a rigor and became collapsed: her temperature was moderately raised during the next four days and she had a slight cough with mucoid expectoration; her subsequent progress was uneventful.

At the same time that she was inoculated, her maid received a similar dose, with the usual consequence of a slight feeling of illness and a trivial temperature twenty-four hours later.

The very severe reaction shown by Mrs. A. to the vaccine suggests that she was sensitized to an organism of the typhoid group, and it may be that at the time of inoculation she was incubating an infection similar to that of her husband: if it were so the vaccine cut short the attack in a remarkable way.

Case 8.—On August 12, 1929, Mrs. W., a lady of middle age and the wife of a doctor, took charge of a young parrot, which was confided to her care by some friends, because it had become sick and she was known to be interested in birds. During the next fortnight the parrot became extremely ill, with vomiting and profuse diarrhœa of a very offensive kind: nevertheless Mrs. W. attended it assiduously and managed to restore it to its owners alive on August 26, but it died three days later.

On September 1, five days after parting with the parrot, she developed a headache and felt shivery: her temperature was found to be 100° F. and she went to bed. During the next five days the fever steadily increased to 103·5° F. and the headache became more severe: it was mainly occipital in distribution, but sometimes diffuse. There was some diarrhœa during the first three days and she frequently vomited, particularly after taking medicine. I saw her first on September 6, in consultation with Dr. T. M. Tibbetts, of Stourbridge. The temperature was nearly 104° F., but the pulse was slow, just over 90 per minute: she complained of intense headache but was mentally quite clear and bright. Some sharp crackling râles were heard in the third left intercostal space, but, apart from this, a dirty tongue and moderate abdominal distension, physical examination was negative. I was at once struck by the resemblance of this case to the one I had seen a year previously, and on inquiry elicited the history of contact with the sick parrot, which warranted a fairly confident diagnosis of psittacosis.

The next day the patient was admitted to the General Hospital: she had slight epistaxis just before she left her home. During the next thirteen days the temperature slowly fell by lysis from 104° F. to normal: the pulse hardly ever reached 100, and respiration was never seriously hurried. Despite the gradual fall in the temperature the general condition appeared to become worse and she was very gravely ill during the whole of the febrile period and for a week afterwards. The signs in the left lung gradually extended: on the 8th instant, rather coarse crepitant râles were heard over the whole of the left upper lobe in front: on the 9th there was definite dullness above the left breast reaching to the axilla and crepitations were heard at the back. Tubular breath sounds were found on the 10th in the left

axilla and coarse crepitant râles were present throughout the whole of the left lung. By the 13th the breath sounds in the left lung became faint and were hardly audible on the 16th ; during the four following days the left lung was almost completely silent and the percussion note over it was dull. A lung puncture on the 18th proved the absence of fluid. Subsequently a few crepitations appeared in the lung and the physical signs eventually cleared up by September 10, when the temperature had been normal for ten days. Cough was never severe but she had a distressing hiccough for some days. There was practically no expectoration. The spleen was never palpable and there were no true typhoid spots (though one suspicious spot was noticed on the flank in the early stages). Occasionally she had diarrhœa and passed loose greenish stools, but this may have been due in part to the measures adopted to relieve abdominal distension, which was of extraordinary severity. She often became acutely distended in the course of an hour or so : injections of pituitrin and eserine with turpentine enemata generally produced immediate relief, with the passage of vast quantities of flatus and a visible diminution in the size of the abdomen, but within an hour she was frequently found to be as tense as previously. On one occasion the passage of a tube led to the escape of so great a quantity of flatus that she had a serious collapse similar to that sometimes seen during operations for the relief of acute intestinal obstruction. Subsequently, to avoid this, the flatus tube was clamped and the gas was allowed to escape slowly. On September 11 she became very drowsy and on the 13th completely stuporose : for six days she never spoke and seemed entirely oblivious to her surroundings. Her face had a mask-like immobility, with a curious retraction of the upper eyelids, so that a wide rim of sclerotic could be seen above the pupils and blinking occurred very seldom. At times slight weakness of the sixth or seventh cranial nerves on the right side was suspected and very severe bilateral ankle clonus was present for several days. The tendon reflexes were exaggerated and on one occasion an extensor plantar response was found on the right side. The fundi were normal, but for one day the right pupil was much larger than the left, though reactions to light were brisk in both. Incontinence was frequent. Her general appearance was suggestive of Parkinsonism, and Dr. Stanley Barnes, who saw her with me, thought there was no doubt of it. As she slowly recovered from the stuporose condition she was completely disorientated in place and time, and later on she told me that she had no recollection at all of this period of her illness. The incontinence persisted for some days after the disappearance of her other nervous symptoms and three weeks after the temperature fell to normal her memory was found to be still impaired. Eventually she made a complete recovery.

Her husband received a protective injection of T.A B. vaccine at my suggestion on September 7, and we gave her three small injections (about 7½ c.c. each) of his serum on September 15, 19 and 20, but they appeared to have no appreciable effect on the course of her temperature. In view of the result of similar injections in Case 9 it is probable that so soon after his inoculation the husband had not accumulated sufficient antibodies to be of value.

Bacteriological Report.—Four specimens of fæces were examined. Those of September 9, 11 and 18 yielded no non-lactose-fermenters. That of the 12th yielded an organism giving gas only in glucose and lactose broth, acid and clot in milk, acid and gas in dulcite, maltose and mannite, and no reaction in saccharose and insulin.

The presence of acid and clot in milk culture renders it possible that this organism, which in some respects is rather like *B. aertrycke*, was in reality a lactose fermenter and, if that be so, all the four specimens of fæces gave negative results as regards *B. psittacosis*. The blood-culture, taken on admission, was sterile and a post-nasal swab yielded no non-lactose fermenters.

The urine (September 7) yielded an organism identified by its sugar reactions in 48 hours as *B. fæcalis alkaligenes*. Cultures from a lung puncture (September 17) produced an

organism which, by the sugar tests, resembled *B. fæcalis alkaligenes*, but which was non-motile and so short that it was impossible to be certain whether it was truly a bacillus or a coccus.

B. psittacosis, then, was not found in fæces, urine, post-nasal swab, fluid from lung-puncture or blood.

B. fæcalis alkaligenes was obtained from the urine (and possibly from the lung).

Agglutination tests against *B. typhosus*, *B. paratyphosus* A and B, *Salmonella* mutton and Newport on September 8 and 10 (in the second week of illness) were completely negative. Serum taken on September 19 however agglutinated 24-hour broth cultures of *B. psittacosis* Perry, National Coll. Type Culture 1 : 500, and the organism *B. fæcalis alkaligenes* from the urine, broth culture 1 : 40, but there was no agglutination with *B. typhosus* or *B. paratyphosus* A or B. On September 26, a week later, another specimen of serum failed to agglutinate broth cultures of *B. psittacosis*, *B. fæcalis alkaligenes*, or *Salmonella* mutton, but with a suspension from an agar culture in normal saline it agglutinated *B. fæcalis alkaligenes* at 1 : 80.

Saturation with either *B. psittacosis*, *Salmonella* mutton, or *B. fæcalis alkaligenes* removed all the agglutination for *B. fæcalis alkaligenes*.

Case 9.—A healthy Jewish girl of 26 played tennis throughout the day of September 10, which was hot and sunny; shortly afterwards she complained of occipital headache and of feeling shivery; for the next four days, although obviously ill and in spite of occasional vomiting and epistaxis (to which she was at times subject) she carried out her usual secretarial work.

On September 13 her temperature was found to be 101° F.; on the 14th it was 103°, and on the following day, when I first saw her in consultation with Dr. B. Herbert, it had risen to 105°. On the morning of September 14, Dr. Herbert found a patch of dullness and faint breath sounds at the base of the right lung and was suspicious of early pneumonia, although he noticed that the respiration was not rapid and that the pulse remained rather slow—it was recorded by a nurse as 104 to the minute, although it was nearer 120 during his examination. These slight signs at the right base cleared up in twenty-four hours and Dr. Herbert asked me to see her as the diagnosis remained doubtful. Her general condition was good though she appeared seriously ill; she complained of occipital headache, slight stiffness of the neck, and had photophobia. Apart from trivial cervical rigidity and some sharp crepitations at the left base, physical examination yielded nothing of importance. In particular Kernig's sign was negative, the reflexes were normal and the fundi were clear; there was no abdominal distension and the spleen was not palpable. There was no known tuberculosis in the family. The history of the onset—a steady rise in temperature, a slow pulse, headache and slight vomiting and epistaxis—together with the discovery of crepitations at the left base (which had been preceded by questionable signs of early pneumonia on the right side), in the absence of splenic enlargement and any mental dullness, led me to suggest the possibility of psittacosis, although Dr. Herbert, who knew the family well, was fairly confident that contact with birds was unlikely.

Nevertheless, on inquiry we were told that on August 30, 1929 (eleven days before the onset of illness), our patient's fiancé had made her a present of two love birds, one of which, at the time of purchase, appeared to be off colour. The vendor, however, was confident that the bird would soon recover, but this cheerful prognosis proved to be incorrect, for it rapidly became worse and suffered from continuous diarrhœa, and a few days later, on the advice of a local bird fancier, it was placed in a separate cage apart from its mate. Despite the unpleasant nature of its disease our patient continued to attend to the sick love bird, and until she herself became ill no one else in the house did much for it: subsequently the bird was cared for by an elderly aunt (Case 10), whose history is given below. The two love birds, when Dr. Herbert and I inspected them, presented a remarkable contrast, for the sick one remained crouched and motionless on the floor of its

cage, with its feathers bedraggled and ruffled: its breathing was obviously laboured and it frequently passed loose stools. Surprisingly enough, it often took food voraciously. The girl and both birds were removed at once to the General Hospital, where the sick bird was found dead in its cage the next morning. The other bird remained healthy.

For the following week the patient was very gravely ill with a high, continuous temperature, which occasionally reached 105° F., and was nearly always above 104° F. despite frequent sponging.

The pulse remained about 120, but towards the end of the week reached 130. The respiration rate was about 30 for the first three days, but later rose to 50 to the minute.

On September 17 my colleague, Dr. K. D. Wilkinson, saw her with me in consultation, and we found a small area of consolidation at the left base. The remainder of the physical examination was negative, apart from the presence of a few seborrhœic spots on the chest; the patient told us that these always became more prominent at menstruation, which began that day and ran a normal course.

She was still mentally clear, had slight cough with scanty mucopurulent expectoration and complained of flatulence and difficulty in breathing. There was no abdominal distension. During the next three days she became progressively worse: mentally she was dull and torpid, but never completely stuporose, although at times there was mild delirium. The cough varied and rarely distressed her: in general she lay absolutely motionless with a curious impassive appearance, which immediately suggested a comparison with Case 8, in whom this feature was much more prominent. This strange passivity (she was "highly strung" by temperament) in mild degree, persisted for some days after convalescence had begun. The signs in the lungs extended rapidly, and by September 21 it was clear that both lower lobes were entirely consolidated: the percussion note was markedly impaired and tubular breath sounds were well heard over them. Respiration was rapid and shallow, and I think it is fair to say that most physicians at this stage would have been content with a diagnosis of lobar pneumonia if the history of the unusual onset and of the contact with the love birds had not been available. The physical signs in the chest persisted unchanged for another two days: on the 21st a lung puncture was done for bacteriological purposes on the right side, and about 3 c.c. of rusty fluid was withdrawn from the pleura—but no more than this could be obtained. On the 23rd inst. there was almost complete silence over the bases behind: the percussion note did not suggest fluid, and I believe that there was at this stage massive consolidation similar to that in Case 8. The breath sounds were faintly audible again on the 24th and were still tubular in character: but for the next two or three days the lower lobes were almost silent. Subsequently resolution took place fairly rapidly. On September 24 my colleague, Dr. Stanley Barnes, examined her and said that "she would do well for a Parkinson," a suggestion with which Dr. T. L. Hardy agreed when he saw her four days later. Throughout her illness the alimentary symptoms were slight: at one time there was unusual salivation—she seemed in her early torpid period to derive some comfort from constantly blowing bubbles of saliva from her lips—but this cleared up after four days. Distension was never marked, though she passed flatus freely: the stools were of a curious greenish colour and frequently loose. Vomiting occurred only very occasionally and she took nourishment well throughout. The urine remained normal. Apart from the curious Parkinsonian appearance, no abnormal nervous signs were discovered. The same plan of treatment was followed in this case as had been tried in Case 8. On September 19 and 20 she received two doses of serum from relatives who had been inoculated with T.A.B. vaccine on September 16. Neither of these injections had the slightest effect on her, and it seemed that insufficient time had elapsed to allow of the production of antibodies. The husband of the other

patient (Case 8), who had been similarly inoculated on September 7, kindly allowed us to use his serum and an intramuscular injection on the 21st of 7·5 c.c. was followed by a drop of over three degrees in the temperature.

After thirty-six hours the fever rose again to 104° F., and a similar injection was followed by a like result: further doses were given at daily intervals, and appeared to bring the illness to a dramatic end some days earlier than might have been expected. The injections were prepared quite simply by allowing 20 c.c. of the donor's blood to clot in a sterile tube, and as much serum as separated was used without any special treatment. Fresh blood was taken on each occasion for the following day's injection. On the chart [exhibited] the various injections of serum are shown—the first two ineffective doses are marked C; the latter ones are marked W.

Bacteriological Report.—Neither sputum, urine, blood nor fæces yielded any organism resembling *B. psittacosis.*

Serum collected on September 16 agglutinated both cultures of *B. psittacosis* (National Collection of Type Cultures) at 1 : 900 (not 1 : 1,000) dilution, and also a broth culture of *Salmonella* mutton at 1 : 500 (not 1 : 700). An Oxford suspension of *Salmonella* mutton was agglutinated at 1 : 125. Negative results were obtained with *Salmonella* Newport, *B. gaertner*, *B. typhosus* and *B. paratyphosus* A and B. A later specimen of blood, taken October 1, failed to agglutinate broth cultures of *B. psittacosis*, *Salmonella* mutton or *B. fæcalis alkaligenes*, but agglutinated suspensions in saline solution of *B. psittacosis* 1 : 20, *Salmonella* mutton 1:40, *B. fæcalis alkaligenes* 1:20. Saturation with *B. psittacosis* or with *Salmonella* mutton left the agglutination unchanged or even slightly improved for any one of the three organisms, but saturation with *B. fæcalis alkaligenes* removed all the agglutination for that organism and left it unchanged or improved for the other two. Serum collected on November 8, when the patient was convalescent, agglutinated similar suspensions of *B. psittacosis* and *Salmonella* mutton in rather higher dilution (up to 1: 100) and an Oxford suspension of *Salmonella* mutton at 1 : 100. There was no agglutination with control normal serum.

Case 10.—On September 15, 1929, as Dr. Herbert and I were leaving the house after our consultation on Case 9, we were told that the patient's aunt, who had cared for the sick love bird for a few days, had become ill and had been sent to bed by her doctor with fever and bronchitis. She was admitted to the Selly Oak Hospital shortly afterwards with a slight temperature (about 100° F.), and signs of bronchitis and possible consolidation at the base of the right lung. As her condition did not appear grave, and as her temperature soon fell to normal, she was transferred to the adjoining infirmary, but was brought back to the hospital when I told Mr. R. P. S. Kelman, the Medical Superintendent, of my suspicions of the possibility of psittacosis infection. Mr. Kelman was good enough to allow me to see this patient in the hospital on September 21. She was a feeble old lady of 73 with signs of emphysema and cardiovascular degeneration. A patch of consolidation was found at the right base, but her temperature was then normal: the respirations, however, were hurried—36 to the minute. Slight vaginal hæmorrhage of uncertain origin had occurred that morning, and the urine contained albumen; nothing grossly wrong was found on pelvic examination. Dr. Hillier found that her blood-serum agglutinated *B. psittacosis* strongly (up to 1 : 500 dilution), and she died a few days later, after developing a fresh patch of consolidation in the left axilla. No post-mortem examination was allowed. It is recognized that, in the elderly, infections of the typhoid group may follow an almost afebrile course, and in view of the history and positive agglutination this case may fairly be regarded as an instance of psittacosis.

Case 11.—Dr. E. H. Alton, of King's Norton, after reading my earlier communication on this subject, furnished me with the following account of a remarkable case that occurred in his practice.

Early in 1926 a middle-aged man returned to Birmingham from West Africa bringing with him three young parrots all of which, within a few days, sickened with

diarrhœa and died. Almost immediately after the death of the last of the birds, the man himself, who had previously been in good health, became ill with continuous fever. At the end of a week he was seen in consultation by one of my colleagues at the General Hospital and a diagnosis of typhoid was suggested. A Widal, however, proved negative. During the second week of illness, extensive signs of pneumonia developed in the right lung and he was again seen by the same consulting physician, who confirmed Dr. Alton's findings and thought the condition was probably due to an unusual influenzal infection. The fever persisted and in the third week the man was almost continually unconscious; the physical signs in the right lung changed and in place of well-marked tubular breathing the breath sounds became inaudible. Dr. Alton needled the chest several times as he thought an effusion had developed, but never found fluid; he was so struck by the silence of the lung that he got his partner, Dr. J. A. Brown, to see the patient and he also explored the chest with a negative result. The man died at about the end of the third week of illness. The spleen was never enlarged and there were no spots. At the time the possible significance of the contact with sick parrots was not appreciated, but the clinical history leaves no doubt that this was in fact a case of psittacosis.

Case 12.—In November, 1929, in consultation with Dr. Smeeton Johnson, of Kidderminster, I saw, on three occasions, a man of middle age, who had an illness that ran a course exactly similar to that of Cases 8 and 9, and my colleague, Dr. L. G. Parsons, who saw both these cases while they were in hospital, and also Dr. Johnson's patient, agreed with me that they were clinically indistinguishable.

This man was a pigeon fancier, and for years he had been daily in close contact with these birds, of which he had over 100 in his own aviary. There was no definite history of contact with sick birds, but Professor C. J. Lewis found that his blood gave a slightly positive agglutination for *B. psittacosis* and a negative result for all the other members of the typhoid and Salmonella group; in addition, the illness was brought to a dramatic end by the injection of serum from a man inoculated some weeks previously with T.A.B. vaccine—exactly as occurred in Case 9. There was a history in this case of the occurrence of a similar illness four or five years previously. The absence of sickness among any of the birds with which the patient was known to have come into contact raises the unpleasant possibility that this disease may be contracted from apparently healthy birds.

Case 13.—On November 23, 1929, a lady, aged 50, purchased a South American parrot which was noticed to be sick on its arrival in her home. The bird developed a nasal discharge, severe diarrhœa and distressed breathing and it died on December 8. Two days later the lady herself became ill and was thought to have a cold. On the 13th her temperature was 104° F. and she had to stay in bed. I saw her first on December 15, with Dr. W. J. Hirst, of Moseley. Her temperature was then 103° F., and her pulse was only 96. She complained of intense occipital headache, radiating down the neck, but physical examination was quite negative apart from the presence of a few scattered râles in the left lung. For the next two weeks she had a continuously high temperature between 103° F. and 104° F., and was often stuporose and completely incontinent. A troublesome cough was present throughout without expectoration, and she had signs of diffuse bronchitis, but there was no definite consolidation; in the third week her temperature fell by lysis to normal for three days and her general condition improved slightly, but on the twenty-seventh day of her illness she relapsed and had a temperature varying between 99° F. and 101° F. for a fortnight; during this period there was definite consolidation at the right base. She now appears to be convalescent but is mentally very emotional and unstable.

Blood-cultures taken on the fifth day of illness were sterile and nothing of significance was recovered from the stools and urine in Professor Lewis's laboratory. The agglutination reactions by Dr. E. Baylis Ash were as follows: On December 15

(fifth day of illness) completely negative to all the typhoid and Salmonella group except *B. psittacosis* Perry, with which there was a positive macroscopic result at a dilution 1 : 15 and microscopic 1 : 10. On December 18, agglutination of *B. psittacosis* was present at 1 : 20 macroscopically and 1 : 40 microscopically. *Salmonella* mutton was also agglutinated at 1 : 40 dilution but all the others were still quite negative. On January 17 (during the relapse) all the agglutination tests were quite negative.

Three small injections of serum from men inoculated with T.A.B. vaccine three months previously were given in the early stages of the illness, and each was followed by a transient fall in the temperature, but it was not possible to arrange for continued treatment of this kind. In the later stages, after the positive agglutination results had been obtained, several daily injections were given of vaccine prepared from *B. psittacosis* cultures but they had no influence on the disease.

Case 14.—This patient was the husband of the patient in Case 13. On December 17, when his wife had been ill for one week, he received, at my suggestion, a prophylactic inoculation of T.A.B. vaccine (100 millions of each organism). Immediately afterwards he had intense pain at the site of injection and an hour later had a rigor, vomited and went to bed. For the next three weeks he had a moderate temperature (usually from 99° to 102° F., but once reaching 104° F.), intense headache and great prostration. The lower lobe of the right lung was consolidated one week after the onset of the illness and there were signs of diffuse bronchitis, to which he had been subject for some years previously. Professor W. H. Wynn saw him in consultation with Dr. Hirst and myself and agreed with the diagnosis.

B. psittacosis vaccine was also given in this case without effect. On January 15, when he was convalescent, his blood agglutinated *Salmonella* mutton (1 : 20 macroscopic and 1 : 40 microscopic), and *B. suipestifer* (1 : 20 macroscopic). Agglutination-tests with all the other members of the typhoid and Salmonella group (including *B. psittacosis*) were quite negative.

This case ran a course exactly parallel with that of No. 7 of this series.

In connection with these two cases it should be recorded that after the death of the first parrot a second similar bird was supplied by the dealer and placed in the same cage which had been thoroughly scrubbed with lysol. This bird was taken to the University laboratory on December 17, and cultures were made from its nose and fæces with negative results. A few days later a nasal discharge developed but there was no diarrhœa. The bird was killed on December 29 and a most exhaustive post-mortem examination was made which showed that its condition was due to a streptococcal septicæmia. No non-lactose-fermenting organisms were isolated from any of the organs and the parrot's blood failed to agglutinate the stock-culture of *B. psittacosis* Perry, and also the cocci isolated from the sputum of the patient in Case 14. It is clear that the illness of this parrot had no relation to the infection of the human cases.

Cases 15, 16 and 17.—These cases, all members of one family, were admitted to the General Hospital under my care at the request of Dr. Hugh Tibbits, of Warwick. A parrot was bought on December 19, 1929, and died unexpectedly on January 1, 1930, without signs of previous illness apart from a questionable nasal discharge. Another parrot was obtained from the same dealer on January 2, and this bird was noticed to be sick at the time of purchase and it died on the following day.

Case 15.—On January 8, A. G., a woman aged 51, complained of headache, drowsiness, and shivering, and she eventually had to take to her bed on the 12th. Dr. Tibbits saw her later and found signs of pneumonia and sent her into hospital with the diagnosis of psittacosis on the 16th.

On admission she was drowsy and apathetic: her temperature was 101 and the pulse was about 100. The percussion note at the right base was dull and

breath sounds were entirely absent over the whole of the posterior aspect of the right lower lobe. Her temperature fell to normal in three days and remained so, except for trivial rises in the evening to about 99° F. for a further four days, and her general condition improved. A few crepitations appeared in the silent area in the lung two days after admission, and breath sounds became audible. There was no cough or expectoration, and no diarrhœa or vomiting. My house physician, Mr. Smallwood, found the spleen palpable on January 22, but I could not feel it the following morning. A blood-count showed a moderate leucocytosis (12,400 white cells, with 83% polymorphs). Nothing of significance was recovered from cultures of the blood, urine, or fæces. Serum taken on January 17 (the ninth day of illness) agglutinated *B. psittacosis* Perry strongly at 1:20 dilution and feebly at 1:50. There was also a feeble agglutination with *Salmonella* mutton, but none with any of the typhoid or others of the Salmonella group, or with *B. fæcalis alkaligenes*.

Case 16.—C. G., aged 58, the husband of A. G. (Case 15), was admitted on the same day as his wife (January 16). He had been ill for five days and almost constantly delirious for three. On admission he was excitable, mildly delirious, cyanosed and obviously very ill. His temperature was 103°, his pulse was rapid (140) and there were signs of consolidation at the right base.

He coughed a little, but there was no expectoration. The spleen was not palpable. The following day his general condition was worse; the right base was dull to percussion and breath sounds were absent; puncture of the chest yielded no fluid. A blood-count showed a leucopenia (6,000 white cells per c.mm.). A few hours later signs of consolidation were found in the left upper lobe and he died on the afternoon of January 18. There was no diarrhœa or vomiting. Cultures from the blood, fæces and urine yielded nothing of significance and there was no agglutination of any of the typhoid or Salmonella group of organisms.

A post-mortem examination was made twenty hours after death by Professor G. Haswell Wilson, of which the following is a report:—

The body is that of a well-developed, somewhat obese man. There are no external morbid appearances.

Thorax.—The pericardial sac is normal. The heart weighs 380 grm. No lesion is found in the valves or cavities. The muscle is rather pale, but is not appreciably softened. The coronary arteries show slight patchy atheroma.

The lungs are free from adhesions. A few minute petechial hæmorrhages are seen beneath the visceral pleura. There is no evidence of pleurisy, except at the right base, where there is an area about ½ in. in diameter covered by a thin pellicle of recent fibrinous exudate. The upper lobe of the left lung is completely consolidated, but the lung is not increased in size and is not marked by the ribs.

The consolidated lung substance is of a dusky red colour and of a dry and almost crumbling consistence. There is no evidence of suppuration, and the appearances are quite unlike those of an ordinary lobar or broncho-pneumonia. The bronchi are congested, and those of smaller size contain a small amount of turbid blood-stained fluid, with no obvious mucopus. The unconsolidated lung substance is poorly aerated, congested and slightly œdematous. Similar changes are seen in the right lung, but on this side the consolidation involves part only of the lower lobe. At the edge of the consolidated area, just beneath the early fibrinous exudate on the pleura, there is a small area resembling ordinary broncho-pneumonia, with a small central bronchus from which mucopus exudes on pressure.

Abdomen.—The peritoneum is normal. The liver, 1,500 grm., is pale from cloudy swelling and slight fatty infiltration. The spleen, 300 grm., is enlarged and very soft. The pulp is intensely congested and is almost diffluent in consistence. The kidneys weigh together 300 grm. The substance is pale from cloudy swelling and the appearance of the cortex suggests the presence of catarrh in the tubules. No lesion is found in the bladder. The suprarenals and pancreas are congested and rather soft. The stomach and intestines are œdematous. The mucous membrane of the stomach shows a few small recent erosions along the greater curvature. The small intestine contains a small amount of slimy bile-stained material, but it is not congested, and there is no change in the lymph follicles. There is slight patchy congestion in the large intestine.

Head.—The pia-arachnoid covering the cerebral hemispheres is opaque and slightly thickened, and the underlying convolutions are slightly atrophied, otherwise no lesion is found in the brain or its membranes.

Marrow.—The femur marrow is almost entirely fatty, but there is a small area of pale very soft red marrow.

The changes in the lung are those of a pneumonia of unusual type and do not resemble those found in lobar pneumonia, in ordinary broncho-pneumonia, or in septic pneumonia complicating a septicæmia due to infection by any of the pyogenic organisms. The condition of the spleen, however, suggests that a septicæmia is present. There is no lesion to suggest typhoid fever or other acute enteric infection.

In view of the changes found in the body I am of opinion:—

(1) That death was caused by pneumonia and septicæmia.

(2) That the appearances are compatible with the clinical diagnosis of psittacosis.

A preliminary histological examination of the sections of the lung by Professor Wilson shows that the affected areas are uniformly consolidated; the exudate is fibrinous, cells are relatively scanty and almost entirely mononuclear. There are scattered areas of congestion and hæmorrhage and here and there small patches of œdema without fibrin. There is no selective perivascular or peribronchial distribution of the exudate as occurs often in influenzal pneumonia. The smaller bronchi are filled with desquamated epithelium; the larger bronchi show a similar desquamation, but quite empty. A certain amount of anthracosis is present in the lung with a slight lymphatic reaction.

A more detailed account of the histology is in course of preparation and will be included in a subsequent report.

An exhaustive bacteriological investigation of this case has been undertaken by Professor C. J. Lewis and Dr. W. T. Hillier. A bacillus in its sugar reactions resembling *B. fæcalis alkaligenes* has been recovered from the lungs and spleen (both from cultures made at the post-mortem examination and from stab cultures made three hours after death).

Professor Lewis has also isolated another type of non-lactose fermenting bacillus from the lung which he thinks may prove to be pathogenic. A complete report will be prepared as soon as possible.

Case 17.—S. G., a man aged 25, son of Cases 15 and 16, was admitted to the General Hospital on January 20. He became ill on January 16 with headache and diffuse pains about the body, but did not go to bed. There was no vomiting or diarrhœa.

On admission the temperature was 105° F., the pulse 110, and the respirations 25 per minute. He was torpid and slightly cyanosed and there were signs of consolidation of the right base, with marked tubular breath sounds. Two days later the affected lung was quite silent over the whole of its posterior aspect. Exploration yielded no fluid. On January 24 a few fine crepitations were heard at the right base but breath sounds were almost entirely absent; at the left base behind, a large area of consolidation with tubular breath sounds was present. Despite the extension of the pulmonary signs the respiration rate was only 24 per minute and there was practically no cough or expectoration. His general condition has improved and his temperature has fallen by lysis to 101° F. A blood-count shows a moderate leucocytosis (9,800 white cells per c.m.m. with 87% polymorphs). Cultures from the blood, urine and fæces show nothing of importance. From the lung puncture a bacillus has been obtained similar to that isolated from the spleen and lung of Case 16.

His serum does not agglutinate *Salmonella* mutton or *B. psittacosis* Perry but it does agglutinate the organism recovered from the spleen of the patient in Case 16 at a dilution 1 : 40.

Review of the Clinical Aspect.

With the four cases described in my first communication [1] those now reported make a total of seventeen, of which five proved fatal.

As a general statement it is fairly accurate to say of the severer cases that they resemble typhoid septicæmia in retaining a relatively slow pulse despite a high continuous fever. Even before the development of the unusual pulmonary signs, however, certain features distinguish them from true typhoid: the onset is usually more sudden and the temperature rises more rapidly. Headache is intense, generally occipital in situation, and often associated with slight cervical rigidity. Epistaxis occurred in one patient. Sweating was sometimes severe. Diarrhœa and vomiting sometimes occur in the early stages, but as a whole the alimentary symptoms, apart from distension, have been trivial. The spleen became palpable in one case, and then only for a few hours: no rose spots have been observed. In one case a typhoid-like relapse occurred. The outstanding feature of the clinical picture is the involvement of the lungs. At the onset signs of slight shifting bronchitis appear, to be followed in a few days by those of extensive consolidation manifested by impairment of the percussion note and the presence of tubular breath sounds. Still later the percussion note becomes completely flat and breath sounds in the affected area disappear. This curious silence of the lung may persist for some days after the temperature has fallen and the general condition has improved. A whole lung may be affected in this way. Resolution occurs very rapidly and completely, and is accompanied by fine crepitant râles.

Repeated explorations of the chest had shown that these signs were in no way due to pleural effusion, and I concluded that they were associated with obstruction of the smaller bronchi. Confirmation of this opinion was afforded by the post-mortem in Case 16.

Certain negative features in the respiratory condition are important. Although cough is frequent and at times incessant it is never painful, and expectoration is scanty and frequently absent: only once was any rusty sputum obtained (Case 5). Respiration is not hurried unless the area of lung involved is very extensive: it was easy and never "pneumonic" in character. Pleuritic friction was never found.

The nervous signs described in Cases 8 and 9 are noteworthy, particularly as they were also marked in Case 12 and to a lesser degree in Cases 15 and 17.

Although the clinical course of most of the cases forms a fairly characteristic picture it is clear from a review of the whole of them that the symptoms and signs may be but slight and equivocal—even when the disease proves fatal (Case 10) and a diagnosis would be frankly impossible unless the history of contact with sick birds was elicited.

The Bacteriological Aspect.

The bacteriological findings are as yet incomplete, and it would be unprofitable to review them at length.

In the earlier part of our investigations a review of such literature as was available led us to concentrate our attention on the discovery of an organism of the typhoid or Salmonella type. In the first case a bacillus corresponding fairly well with this group was recovered from a local parotid swelling, but in none of the subsequent cases have we had any success up to now. A remarkable feature is the recovery of an organism similar in its sugar reactions to *B. fæcalis alkaligenes* from the lung of Cases 8, 16 and 17.

In addition to the investigations already described, a most careful search was made of the body of the love bird responsible for the infection of Cases 9 and 10, both by Dr. Hillier, and in the laboratory of Professor C. J. Lewis, at the University

of Birmingham. *B. psittacosis* was not found, but an organism resembling *B. fæcalis alkaligenes* was recovered from the heart blood, the trachea, the crop, and the bone-marrow. From the crop a bacillus was obtained which gave no acid in dulcite, lactose, maltose, marmite or inulin; acid however in milk, and acid but no gas in glucose and saccharose. From the fæces of the live love bird, the mate of the dead one, on one out of four occasions a bacillus was obtained showing absence of sugar reactions in the manner of *B. fæcalis alkaligenes*, except that after some days the glucose broth had become acid. The bird has never shown any signs of illness, but died suddenly a few weeks later. Whether or not this organism is responsible in any way for human infection is a problem still under investigation.

The results of the agglutination tests are extremely irregular and capricious. In two cases (1 and 5) positive agglutinations to a typhoid organism were obtained, but in nine others there was none. We feel that not much reliance can be placed on the positive agglutinations with *B. psittacosis* or the Salmonella group generally as a means of exact diagnosis, particularly when, as in this series, they were often so transient and variable. This matter also must be one for further inquiry.

Conclusion.

A critical survey of these cases leads almost inevitably to the conclusion that serious illness in men may be due to contact with sick parrots or love birds. The history of Case 12 suggests that apparently healthy birds may also occasionally be responsible for human infection.

It must be admitted that the exact means by which the disease is transmitted to man still remains obscure, and I have anxiously considered the possibility that the association with sick birds in these cases was nothing more than a strange coincidence. That facile explanation must, I think, be rejected for the following reasons: (1) The association of sick parrots with unusual forms of human illness was recognized forty years ago, and a considerable number of cases of this type have since been reported at varying intervals from different parts of the world, though strangely enough very little attention has been given to the matter in this country. (2) The clinical course of the cases described conforms with none of the ordinary types of pneumonia or typhoid or infection with the Salmonella group. (3) The post-mortem findings in Case 16 are suggestive of an unusual form of septicæmia with involvement of the lungs of a distinctive character, which Professor Haswell Wilson had not previously encountered. (4) The number of cases that have come to my notice seems to be too large to permit the hypothesis of coincidence, and, as I have already said, since the publication of my first paper on this subject [1] a considerable number of histories of illness have been sent to me which warrant the opinion that they were in fact instances of this type of disease. Of these I have only included one (Case 11) in this series.

In view of the predominance of the parrot as the agent of infection, the retention of the name "psittacosis" for this group of cases is justifiable at the present time, but is it correct to assume that it is a specific disease due to a particular micro-organism? The clinical similarity of the cases and the singular post-mortem findings suggest that it well may be, but certain considerations render a complete acceptance of that position impossible.

Perry's investigation [4] showed that parrots might be heavily infected with an organism almost indistinguishable from *Salmonella* mutton. It is this organism which is preserved in the National Collection of Type Cultures as *B. psittacosis*. So far as I am aware, no case of human infection followed contact with his birds, but obviously it was possible, and had it occurred the symptomatology might have been quite different from that recorded in my cases in which *Salmonella* mutton has not been found.

There is, further, the result of the examination of the second parrot associated with Cases 13 and 14; in this instance the bird died of a streptococcal septicæmia, and human infection from it is a possibility which cannot be denied.

Finally, is psittacosis as rare a disease in this country as the scanty references in the literature suggest? The fact that cases have come to my notice at fairly regular intervals since my attention was first directed to the matter and that Case 11 occurred in 1926 strongly support the view that similar types of infection have prevailed in England and that they have not been hitherto recognized.

REFERENCES.

[1] THOMSON, A. P., *Lancet*, July 20, 1929, p. 115. [2] MCCRAE, T., "Modern Medicine" (1925), Osler and McCrae, i, 128. [3] MCCLINTOCK, A., Publication No. 1 of McClintock Foundation, New York, 1925, "Pleomorphism in Bacterial Protoplasm. A Study in Psittacosis." [4] PERRY, H. M., *Brit. Journ. Exper. Path.*, 1920, i, 131.

Discussion.—Dr. ROBERT HUTCHISON said: I have been in touch with about twenty cases of psittacosis, mostly in the London area, during the last three months; in three of these the patients have died. The cases have nearly all occurred as "house epidemics," two or more persons being affected in a house in which there has been a sick parrot. With one exception all the parrots have been of the green Amazon variety. The incubation period of the disease seems to be about ten days and infection has nearly always been from the bird direct. In one case, however, a patient seemed to contract the disease by nursing her sister who was already affected.

I have little to add to the clinical description given by Dr. Thomson. The cases all suggested a typhoid infection in their general character. Headache was often a prominent symptom at the outset, and in a few cases there was epistaxis. The pulse tended to be slow and the spleen was never palpable, but in at least two there were small rose spots. Diarrhœa was never prominent. The lungs became affected more or less in all, but in no case have I seen the very dense consolidation spoken of by Dr. Thomson. Usually there were moist sounds at one base or both, with some impairment of note only. In one case there was pleurisy, which was verified post-mortem, along with a peculiar form of pneumonic consolidation, apparently like that which Dr. Thomson has described.

The diagnosis in every case was made on circumstantial grounds, as all bacteriological tests proved negative. To anyone who has had experience of the disease, however, its recognition is not difficult. The combination of a clinical picture resembling a typhoid infection, but without positive agglutination, with signs in the lungs suggesting an atypical pneumonia in a person who has been recently in contact with a sick parrot is conclusive enough.

There is as yet no specific treatment for the disease; with regard to prophylaxis, it has been suggested that parrots should be quarantined after their arrival in this country to make sure that they are in good health before they are sold. As to this, though in most of my cases the parrot had been recently acquired, yet, in one, the bird had been purchased three months before the disease appeared, and is said to have arrived at the dealers two or three months before that. There is reason to believe that the infection has come to Europe from the Argentine, where there was a serious outbreak of psittacosis last July.

Dr. G. T. WESTERN said that at the London Hospital during the last few weeks they had investigated twelve cases of this disease and six parrots which were reputed to be responsible for some of these cases. Bacteriological examinations both in the patients and in the birds had failed to show the presence of any member of the Salmonella group. Serologically no evidence of the presence of any member of this group had been obtained. Taking these negative results into consideration along with the almost complete absence of evidence of Salmonella infection in epidemics of psittacosis in man since the disease in parrots was first investigated by Nocard, he had been led to consider the possibility of the disease in man being caused by a filter-passing virus transmitted from parrots. He had been fortunate in securing the collaboration of Dr. S. P. Bedson in this investigation.

Dr. S. P. BEDSON said that when he joined Dr. Western in his investigations of this disease at the London Hospital, it had become clear that the causal agent was not one of the Salmonella group. The possibility that a hitherto unrecognized filterable virus was responsible very naturally occurred to one, and experiments were designed to see if this were so. The experimental reproduction of the disease in birds was first attempted, and this, of course, entailed the choice of a suitable experimental animal. The parrot was ruled out, not only because of its cost, but also because the parrot population of the shops appeared to be a sick one. The budgerigar, or so-called "love bird," was selected because the available stocks appeared healthy and were reasonable in price, and because this species was reputed to be susceptible to the disease. In view of this last point the stock of normal birds was housed in a different room from that in which birds on experiment were kept. The starting point of these experiments was a parrot which had been the cause of two human cases. It was ill when received and died a day or so later. No marked changes were observed post-mortem, and anaërobic and aërobic cultures made from the different tissues on a variety of media gave no growth. An emulsion of spleen, liver and intestine inoculated intraperitoneally in budgerigars resulted in their death in five days, and the same result was obtained with the emulsion after filtration through a Chamberland L.1 bis candle. Controls inoculated with the unfiltered emulsions which had been heated to 100° C. for twenty minutes remained well. It had been possible to pass the condition to other budgerigars with the filtrate of an emulsion of the organs of one of the birds succumbing to the inoculation of filtered parrot material; controls inoculated as before remained well. It was recognized that the parrot was susceptible to the virus of fowl-plague, so that the possibility that one was dealing with this virus had to be kept in mind and was made the subject of experiment. Man was said to be insusceptible to fowl-plague, but reliable evidence on this point was lacking. Material from four human cases of psittacosis had been inoculated in budgerigars which were still under observation. Some of these birds appeared to be ill, but the final outcome of the experiment could not be predicted. Further parrot material was also being examined. It was not claimed that this virus which had been isolated from the parrot was the cause of the disease in man, but in view of the strong circumstantial evidence connecting diseased parrots with the disease in man, and the fact that the isolation of this virus was the only positive finding obtained, this was not improbable.

Dr. E. D. MACNAMARA said: On December 21, 1929, a parrot arrived at my house as a Christmas present for two small boys. It appeared to be in a sickly state and died on December 30, 1929. Three persons who had been staying in the house and had been in contact with the parrot fell sick January 7, 1930, with symptoms of psittacosis. A fourth person, a guest, who had arrived in the house on December 30, 1929, after the parrot had died and been removed to an out-house, sat in a chair close to the place where the bird had been. Symptoms of psittacosis developed on January 10, 1930. A fifth person, a gardener, who had not been in contact with the parrot when it was alive, but had handled it when it was dead and had cleaned out its cage, developed symptoms of psittacosis on January 10, 1930. These two last cases point precisely to an incubation period of ten days. It is remarkable that the two boys to whom the parrot had been given and who had assiduously tended it until its death have not so far (January 29, 1930) shown any symptoms. Numerous persons who have not been in contact with the parrot, but have been in close contact with the patients who had been infected by the parrot have, so far, presented no symptoms.

Dr. LEVY SIMPSON said that in those cases in which there had not been direct contact with the parrot it was possible that the parrot's fæces, which were known to contain the infective agent, became dried and disseminated as dust particles.

With regard to the incubation period: in many of the cases investigated from the London Hospital it had not been possible to fix a definite time, but in some of them it was quite certain that the period was ten days. This was in keeping with the investigation of previous epidemics: 1880 (Ritter), 9 to 14 days; 1893 (Dubief), 9 days; 1896 (Gilbert and Fournier), 8 to 9 days; 1917 (McClintock of Pennsylvania) 7 to 12 days.

Evidence in the literature on the question of man-to-man infection was not very convincing, although Nicolle, 1898, described infection of a nurse. There was only one case in the London Hospital series where this mode of infection was probable.

Although cases of psittacosis had occurred here and there for some years, and others were perhaps unrecognized, it was nevertheless extremely probable that the present European epidemic could be directly attributed to shiploads of diseased parrots from the Argentine.

In July, 1929, there was an outbreak of psittacosis in the Argentine. The nature of this remained unrecognized for some months, but by October, 1929, the number of cases in man is said to have increased to several hundreds, thus constituting the largest epidemic yet recorded. Of the cases investigated at the London Hospital nearly all, but not all, the parrots were recently imported and were of the green Amazon variety that comes from South America. It would therefore appear that the sequence of events in this European epidemic is a repetition of that which occurred in 1892, when Dubois and Marion set sail from Buenos Aires for Havre with 500 parrots, of which 300 died on the voyage. The remaining birds were directly responsible for the Paris epidemic of 1892, in which fifty people were attacked by psittacosis and sixteen died. It was then believed that the conditions of the voyage and of the packing were responsible for the actual production of the disease in parrots. In view of the 1929 South American epidemic it would seem more accurate to state that these conditions are responsible, not for the initiation, but for the spread of the disease from those parrots already affected to a large proportion of the rest of the consignment.

Section of Therapeutics and Pharmacology.

[*December* 10, 1929.]

DISCUSSION ON THE USE OF PHENYLHYDRAZINE IN THE TREATMENT OF POLYCYTHÆMIA.

Dr. F. Parkes Weber: I have recently been interested in a patient with erythræmia accompanied by variable chronic, sometimes fairly deep, jaundice, the jaundice apparently representing part of a conservative reaction—an attempt to lessen the polycythæmia rubra by excessive destruction of erythrocytes in the enlarged spleen.[1] In that case, treatment by phenylhydrazine seemed scarcely advisable, since by further destruction of erythrocytes in the body, it might not only increase the jaundice but also favour the tendency to formation of bilirubin calculi—which are of not exceedingly rare occurrence in the subjects of familial hæmolytic icterus. I thought it might even produce hepatic cirrhosis, which is known to have developed in several erythræmic cases even without phenylhydrazine treatment.[2]

However, patients, as a rule, prefer treatment by drugs to treatment by periodic blood-letting, and perhaps a cautious trial of phenylhydrazine therapy might be made in the above-mentioned case. Recently, I found that an erythræmic man who had been improved under my care by blood-letting, was being treated at another hospital by benzol. I had feared to try phenylhydrazine in that case owing to decided albuminuria. At the present time I am cautiously treating a typically erythræmic man in hospital by phenylhydrazine, in spite of a definite history of previous renal colic.[3]

Dr. Terence East showed a chart illustrating the effect of phenylhydrazine in treating a case of polycythæmia. The man was 52 years old and had had symptoms of headache and giddiness for several months. *Blood-count*: Red cells 9,000,000, hæmoglobin 130%, colour-index 0·73. White cells 10,000 (*Differential*: Polymorphonuclears 78·5%, eosinophils 1·0%, lymphocytes 18·5%, large mononuclears 2·0%). Van den Bergh indirect test 0·2 units. After a period of observation, 0·1 grm. of phenylhydrazine was given thrice daily in a capsule for twelve days, so that a total dose of 3·6 grm. was administered. There was soon considerable jaundice and a great decrease in the red cell count and the hæmoglobin. The lowest level was reached on the twelfth day after stopping the drug, although the decrease had already begun, a few days before the drug was discontinued. The effect took about a week to appear. When the red count was at its lowest there was a leucocytosis of 22,000. After a period of regeneration lasting just over six weeks, in the early phases of which the reticulocytes were numerous, reaching 12%, the blood-count was again at about the same level as before the treatment. The jaundice was at its height after the drug had been given for twelve days. The pigment always gave the indirect van den Bergh reaction, attaining a level of three units. In order to avoid the severe effects of the large dose, smaller doses were

1 F. Parkes Weber, *Brit. Med. Journ.*, 1929 (ii), p. 892.

2 On the causation of the hepatic cirrhosis in such cases, with or without phenylhydrazine treatment, see E. Levi, *Zeitschr. f. klin. Med.*, Berlin, 1924, c, p. 777.

3 Albuminuria of slight or moderate degree has often been observed in erythræmic patients. Renal calculi have been much less frequently recorded—see the case described by Weber, Barker, Adams, and Dickson, *Brit. Med. Journ.*, 1928 (ii), p. 1129. Nephro-lithiasis was present in a case of erythro-leukæmia, of which Professor T. R. Elliott has kindly given me details (the connection of uric acid calculi with leukæmia is, of course, well known).

next given, viz., 0·45 grm. in two days, then after a week, 0·3 grm. in two days, followed by the same doses at the same intervals. The red cells were thus kept at about six millions and the hæmoglobin at about 120%, and there was no increase in the van den Bergh reaction to any extent, although it ranged round one unit of indirect pigment. After giving no drug for a month, the red cells were once more over eight millions, and the hæmoglobin 140%.

The blood-pressure, which was 160/115 before the initial treatment, fell to 100/75. It is now rising again.

It will be seen from these observations that adequate doses of phenylhydrazine will cause a fall in the red cells, but at the expense of rather violent blood destruction. Small doses, often repeated, will restrain the tendency for the count to return to its usual high level. But that tendency is always there, and it remains to be seen whether it is feasible to give a potent protoplasmic poison, such as this drug is, indefinitely.

DISCUSSION ON THE USE OF NIRVANOL IN THE TREATMENT OF CHOREA.

Dr. Bernard Schlesinger: At the moment we have no right to speak of nirvanol as in any way a cure for acute rheumatism, but its effect in certain cases is so remarkably beneficial that further trial and investigation of its mode of action are fully warranted.

The general effect of nirvanol may apparently be produced in nearly every patient and not merely in the rheumatic subject.

In most cases, from eight to fourteen days after a daily oral administration of 0·25 to 0·3 grm., a well-marked morbilliform eruption appears, usually accompanied by pyrexia. The temperature may be considerable for several days, rising as high as 104° F. in some instances, but in the majority of my cases moderate or quite mild degrees of pyrexia were observed, and at times the patients remained afebrile throughout. The rash which, in tinge and character, bears a certain resemblance both to morbilli and rubella, may best be described as falling between these two exanthemata. Occasionally it may assume a scarlatinal or an urticarial form. After about four or five days the eruption disappears, leaving behind no trace and not being followed by desquamation. There are few subjective symptoms, beyond a mild pharyngitis and cervical adenitis in some cases, and slight drowsiness and headache in others. The rash may irritate slightly, but in most instances there is no complaint whatever, even when marked pyrexia is present.

Administration of the drug produces almost constant changes in the blood, of which the most important is a true eosinophilia. In addition there is generally a leucopenia, with decrease in the polymorphonuclear cells, and a relative lymphocytosis and monocytosis. The alteration in the blood-count is only temporary, and when the reaction is over and the drug is stopped, the blood picture gradually becomes normal.

A number of cases have no febrile reaction and no rash, but only show an eosinophilia, while some patients do not react at all.

Treatment of Chorea.—For the successful treatment of chorea by this drug one must aim at producing a nirvanol reaction. With this in view a sufficiently large dose must be given, but at present this is empirical, and there is as yet no means of regulating the severity of the reaction. I have used a daily dose of 0·3 grm. for children of from 9 to 14 years of age, with a correspondingly smaller quantity below

this age (about 0·25 grm. from 6 to 9 years). It is wise never to exceed a daily dose of 0·3 grm., and I have found this sufficient to produce a typical reaction in a woman aged 20. The drug must be stopped immediately a rash or sudden pyrexia appears, and if this has not occurred by the twelfth day it is useless and even dangerous to proceed with the treatment.

In most cases the effect of the drug on chorea is very striking. Just before the onset of the reaction, i.e., usually after about a week or ten days of treatment, the choreic manifestations are aggravated, but with the disappearance of the rash they subside with dramatic rapidity, and are generally almost entirely arrested within a week or ten days. This improvement bears no relation to the stage of the acute chorea at which the treatment was begun, and it appears possible to cut short the illness at any time. I have found that the most successful cases have been those with the most marked reactions, and I have failed to influence the course of the disease when, in addition to the non-appearance either of pyrexia or a rash, eosinophilia has not occurred. Even with a typical reaction, nirvanol may fail, especially in an obstinate case of subacute chorea. The most dramatic improvement is generally seen in the severest and most acute cases, but I have also had successful results with this drug in long-standing chronic cases, which other previous therapeutic measures had failed to influence.

The treatment has not been long enough in practice for us to form any opinion as to the ultimate prognosis, or to gather whether the common liability to subsequent attacks is prevented. Relapses have been reported at varying intervals after the first successful nirvanol treatment, and I have seen two such cases. Should this occur nirvanol will again arrest the chorea, although with this second course the only obvious signs of a reaction is an eosinophilia, and the rash and temperature are not encountered.

Although all the cases I have treated have run a mild and unalarming course, it is only fair to mention that dangerous and deleterious effects of the drug have been reported. For example, Keller describes a case in which a secondary reaction occurred eleven days after the first one, in which gingivitis, tonsillitis, stomatitis, nephritis, jaundice, blood-stained diarrhœa, swelling of the face and œdematous ulceration of the upper lip occurred. Fortunately the patient ultimately recovered. There was some reason to believe that this formidable secondary reaction was brought on by accidental exposure to sunlight. This may have been a coincidence, but since another severe secondary reaction has been reported after giving artificial sunlight to a patient who had just finished his course of nirvanol, it appears wise to guard against such rays for two or three weeks after this form of therapy.

One other clinical manifestation may cause alarm during administration of the drug in a bad case of chorea. Aggravation of the symptoms just before the reaction occurs has already been alluded to, and when the chorea is associated with much mental excitement and hysteria, the mental instability also may be temporarily increased. This occurred in one case to such a degree that the child's mentality was completely altered for a week or more, but after this temporary and somewhat alarming phase the boy became normal again and has remained so since.

Judging from the many accounts from various independent sources, since Roeder's original communication in 1919, nirvanol certainly seems to be a potent drug which is effective in chorea and has the advantage of oral administration. Against this is the fact that there is a small element of risk in the treatment, and for this reason it may be considered unjustifiable to take such heroic measures to combat a self-curable disease.

Realizing this criticism, I have for the last few months devoted my attention to a further aspect of the question, and have endeavoured to discover whether the drug is merely anti-choreic, or alternatively, could in any way be termed anti-rheumatic.

Treatment of Acute and Subacute Rheumatism.—We are all agreed that one of the most obvious manifestations of activity of a rheumatic infection is the presence of nodules and I have been able to watch the effect of the drug in six such cases. I shall endeavour to show that nirvanol seems to have a striking effect both on the smouldering temperature and rapid pulse-rate that may be present, and also on the nodules, causing them to disappear with a remarkable rapidity.

Since, however, nodules may arise in one night and disappear with almost equal rapidity, we must not be led astray and in our enthusiasm substitute "propter" for "post," and, without question, eulogize the drug. Cases have been chosen, therefore, in which the nodules were obstinately persistent and had been observed for a considerable period before the drug was administered.

The results in several cases of this type are very suggestive, if not absolutely convincing; nirvanol commonly has the power of making most of the nodules vanish at about the time of the reaction to the drug, whilst usually one or two, after diminishing to a marked degree, still persist for some weeks until they also finally disappear.

The termination of a persistent mild degree of pyrexia and tachycardia is additional evidence of the beneficial action of the drug against the infection.

In one of the severest of my cases, in which there were very large and widespread nodules, administration of nirvanol caused the nodules and other signs of rheumatic activity to disappear in a striking manner, but the infection was only temporarily suppressed, and fresh manifestations of rheumatism appeared soon afterwards with a return of nodules. A second course of nirvanol acted like the first, the temperature and pulse-rate dropped immediately, and, after a slightly longer interval, the nodules almost disappeared. The rheumatic infection, however, had not been entirely overcome, so that a few nodules persisted and the pulse-rate gradually rose again. A third course of nirvanol was given, and the patient now seems to be well on the road to complete recovery. Nirvanol has certainly failed to influence the rheumatic process in other similar cases.

Nevertheless, after observing these cases, one cannot help feeling that nirvanol, if wisely administered, has a healing effect not only in cases of chorea but also in acute and subacute rheumatism in general.

It is not unlikely that Aschoff's nodes in the myocardium are also made to vanish, seeing that their larger cousins under the skin are influenced in such a striking fashion. Clinically the signs of endocarditis have not been observed to alter under this form of treatment, but one would not expect much change in an old-established lesion. On the other hand, in one or two cases in which the carditis was more acute, the area of cardiac dullness was found to diminish at the same time as other signs of rheumatic activity subsided after the nirvanol treatment.

How the drug acts is still a complete mystery. A possible hypothesis is that it whips up the patient's natural powers of defence. For the moment we can only regard the use of nirvanol as an interesting piece of empirical therapeutics which seems worthy of further study.

Dr. F. J. Poynton: My attention was drawn to nirvanol by Dr. Schlesinger in May, 1929. Since then I have been intent upon studying its effect on chorea, and am now commencing with slow caution to make further investigations upon other rheumatic manifestations and forms of rheumatism.

I regard most cases of chorea as rheumatic, and, though I am not entirely satisfied on the point, I believe that a rheumatic meningo-encephalitis is the best pathological explanation. It follows that in its active treatment there are two lines of approach. The first is the treatment of chorea as a rheumatic lesion. I have tried most of the anti-rheumatic drugs, anti-sera and vaccines, and both combined, during the past twenty-five years, and I have not convinced myself of a specific remedy.

The other practical line is the treatment of the nervous disturbances. Here again I have tried numerous drugs. For a long time I thought chloral and bromide the most useful, but lately I have settled upon chloretone as rather better.

There are two points to which I would allude. One is that chorea, like all other cardinal manifestations of rheumatism, is very variable in both severity and course, and consequently, I look upon reports of successful treatment based upon a few cases as of no essential value, but accept the well-known generalization that acute cases tend to get well more rapidly than the subacute. The other, an important one, is that though I have had many hundreds of cases of chorea under my observation, I have only known two patients die from chorea alone. Some few I have seen nearly die, and we all know that chorea and carditis may be fatal. The purport of this is, that if we treated our cases of chorea by rest and nursing, few, if any, of the patients would die, and that remedies which are in themselves dangerous adventures are not applicable to the condition. This was my attitude when nirvanol was brought to my notice, and I decided to try it after a study of the evidence put before me, because there appeared good support of its direct effect upon the nervous symptoms, and also because its remarkable effects upon the blood and general condition made it reasonable to believe that it might have a deeper influence upon rheumatic processes than one could realize without personal trial. I was fully aware of possible complications. Up to the present, although I have used it in about thirty cases, I have never had any reason for anxiety, but have, as yet, never departed from a dosage of 0·3 grm. per diem for a child aged 9 years, and 0·25 for a child under 9, given orally, half in the morning and half in the evening. When the rash appeared I always stopped the treatment, and when the rash did not appear I never continued the treatment beyond the fourteenth day. The general reactions in my cases corresponded with those described. There was in one case a fleeting jaundice, but I have seen jaundice with chorea on more than one occasion long before using this drug, and am not prepared to say it was due in this case to the drug, but made a mental note of the occurrence. I have had a good many cases in which there have been no rash and no obvious reaction. These have improved, but less definitely than those in which there has been good reaction. I have seen two relapses in cases in which there has not been a reaction, and though each time they improved under the treatment, in the second course they gave no more sign of reaction than in the first. Whether this drug prevents future attacks when in the first instance it has produced a definite reaction and a good result, it is too early yet to say. It is not easy to assess its value, for the reason that the symptoms often increase before the tenth day, and then the quiet after the storm naturally produces a somewhat dramatic effect upon one's consciousness. I am nevertheless of opinion that recovery is more rapid, and that the child becomes steady sooner, than under any other treatment I have used. The nurses in my children's wards have been impressed, and they are good observers, but only weight of evidence and time will give us a sure answer.

I intend at present to continue its use and cautiously explore its possible value in other rheumatic lesions and rheumatic disorders. I believe that it acts on the nervous—rather than on the rheumatic factors—of the disease, but I am approaching its clinical study with an entirely open mind and with only one precaution, which is to do nothing reckless.

Dr. Terence East: The following three cases illustrate the effects of nirvanol in the treatment of chorea :—

(I) A girl, aged 12. Severe case with chorea for many months. At first 0·15 grm. was given twice daily for four days. Then the dose was increased to 0·225 grm. twice daily for three days, and then to 0·3 grm. twice daily for another three days. During this time the chorea increased; when the rash appeared the drug was stopped. Preceding the appearance

of the rash, the heart rate rose during three days. Two days after the nirvanol reaction there were pains in the limbs, and the temperature went up but was speedily controlled by salicylates. Afterwards the chorea was very much less, but was still present. In this case the typical reaction was preceded by a steady increase in the rate of the heart, and was followed by an exacerbation of rheumatism. In all 2·65 grm. of nirvanol was given in nine days.

(II) A woman, aged 20. Dosage at first 0·15 grm. twice daily. Increased to 0·26 grm. twice daily after four days. On the eleventh day the patient became very drowsy. During the preceding days the chorea had become much less and the heart rate had slowed. On the thirteenth day the drowsiness diminished, and further doses of 0·15 grm. twice daily were given for seven days. During this time all trace of chorea disappeared. Eosinophil count, 6·6%. This patient had no fever and no rash, so that it is possible for a good result to be obtained from nirvanol without provoking the reaction. In this case 5·46 grm. in all were given.

(III) A boy, aged 8. Here 0·15 grm. was given daily, in two doses of 0·075 grm. After seven days (0·95 grm. in all having been given) drowsiness appeared, and the rash came out on the following day with a rise of temperature. During the administration of the drug there was a steady increase in the heart rate, which finally reached 160, when the fever was 101·4. The chorea then diminished and the patient was cured.

These three cases illustrate the varied effects which may be produced by the administration of nirvanol. Although good results may be obtained, the use of the drug requires the closest supervision and care, until more is known about it.

[Charts of the cases were shown on the screen.]

Section of Ophthalmology.

CLINICAL MEETING HELD AT THE ROYAL LONDON OPHTHALMIC HOSPITAL ON DECEMBER 13, 1929.

Macular Degeneration in both Eyes.—J. H. DOGGART, F.R.C.S.

G. B., female, aged 28.

History.—Rheumatic endocarditis thirteen years ago; lupus of face three years ago. Sight failing for three years. Attended Mr. C. B. Goulden's Out-patient Department at the London Hospital, December, 1929.

Examination.—Under H. and C.: Right vision, with + 1·5 cyl., 180° = $\frac{6}{36}$ (1 l.). Left vision, with + 1·5 sph. = $\frac{6}{24}$ (2 l.).

At each macula there is an appearance of small, closely-set, glistening crystals. Numerous Tay's spots can be seen in the periphery of both fundi. Vessels healthy. Mentality slow.

I am indebted to Mr. C. B. Goulden for permission to show this case.

Band-shaped Opacities of both Corneæ, arising in previously Healthy Eyes.—J. H. DOGGART, F.R.C.S.

A. G., male, aged 62.

History.—June, 1928: Attended Mr. W. S. Duke-Elder's Out-patient Department at St. George's Hospital, complaining of increasing mistiness of vision during the previous two years. Right vision, with − 1·5 sph. = $\frac{6}{18}$. Left vision, with − 1·5 sph. = $\frac{6}{12}$. Later, vision deteriorated to $\frac{6}{60}$, right and left.

Treatment.—February, 1929: Left cornea scraped. June, 1929: Right cornea scraped. Present vision: Right, with − 0·75 sph. = $\frac{6}{12}$ (4 l.). Left, with − 1·75 sph. = $\frac{6}{12}$ (3 l.).

I am indebted to Mr. W. S. Duke-Elder for permission to show this case.

Band-shaped Opacity of Left Cornea.—J. H. DOGGART, F.R.C.S.

F. B., a boy, aged 12.

History.—Suffered from fits until the age of 2 years. Left eye began to deviate inwards at the age of 3.

1922: Attended Mr. A. C. Hudson's Out-patient Department at the Royal London Ophthalmic Hospital when aged 4. Right eye: normal. Left eye: cornea smaller than in right; iris lighter than in right; fixation defective; floating vitreous opacities; pigmented connective tissue on and near disc.

1925: Right vision = $\frac{6}{6}$. Left vision = hand movements at 0·5 m. Left eye, marginal opacity of cornea. Aqueous albuminous. Lens showed pigment on anterior capsule, and exudates on posterior capsule. Many vitreous opacities. Massive retinal hæmorrhages and exudates.

1926: Left retinitis proliferans with extensive new vessel formation.

1927: Left eye soft, lens opaque. Band-shaped opacity, which subsequently increased.

This patient is now under the care of Mr. W. S. Duke-Elder, to whom I am indebted for permission to show him.

Discussion.—Miss IDA MANN said that she had seen the boy some time ago, when he was under Mr. Hudson's care, and she wondered whether the opacity had been scraped off, for at that time it had appeared to be much denser than it was now.

Mr. DOGGART (in reply) said that there was no note of the cornea having been scraped. It was possible that some of the superficial opacity had dropped off.

Right Corneal Degeneration in Region of Palpebral Fissure, associated with Rigidity of Eyelids.—J. H. DOGGART, F.R.C.S.

A. K., a married woman, aged 45.

History.—Amputation of left breast for carcinoma two years ago. Teeth extracted nine months ago. Attended Mr. R. R. James's Out-patient Department at St. George's Hospital last week, complaining of irritability of right eye during the last six months. Occasional haloes in the evening for the last few weeks.

Examination.—Right vision, with + 2 sph. = $\frac{6}{12}$ (2 l.). Left vision, with $\frac{+3}{+0{\cdot}75}$ 135° = $\frac{6}{5}$. Right pupil elliptical in shape, with long axis horizontal. Both pupils react normally. Tension normal right and left. Fundi normal. No corneal anæsthesia. Fields full.

Examination of accessory sinuses by Mr. L. Colledge: negative. The right upper and lower eyelids are comparatively rigid, so that the patient, unless she squeezes hard, cannot completely close the right eye.

A ridge of raised epithelium extends transversely over the exposed portion of the right cornea. To the nasal side, above the transverse ridge, there are a few punctate areas of raised epithelium. Immediately above and below the ridge can be seen some ill-defined deeper opacity, partly in the form of vertical white streaks. In the right iris, some dilated vessels are visible with the loupe.

The patient is not yet able to tolerate slit-lamp examination.

I am indebted to Mr. R. R. James for permission to show this case.

Miss IDA MANN said that she understood that the patient had had her breast removed for carcinoma two years ago. She thought the condition of the right eye could be accounted for by a secondary carcinoma in the orbit. There was a solid mass behind the right eye which was preventing movement of the eye and lids, and the skin was adherent to a solid mass below the eye. She had seen a similar case of secondary carcinoma in the lower lid from a breast tumour, but in that case there were also deposits in the iris and choroid. Radium might relieve the tightness of the lids. The corneal condition was undoubtedly secondary to the rigidity of the lids.

Parinaud's Conjunctivitis.—G. G. PENMAN, F.R.C.S.

Patient, a boy aged 13, first seen at the Royal Westminster Ophthalmic Hospital, November 16, 1929, with a month's history of "mumps" and redness of the left eye. Temperature had been 100° F. for first three or four days of illness. No pain. On examination: Both lids of the left eye were swollen, and the upper lid was much thickened. There were many follicles on the conjunctival surface of the lower lid, and the ocular conjunctiva at its outer part showed much thickening of a brawny character, and was extensively injected. The cornea was clear. On eversion of the upper lid, a mass of large follicles was displayed, with a whitish patch of ulceration towards the upper and nasal part of the tarsal plate. This eye also showed a concomitant convergent squint, which had been present since babyhood. The pre-auricular gland was greatly enlarged, with a smaller gland just beneath it, with some swelling of the parotid, giving rise to the likeness to mumps. There was also a swelling of a small cervical gland just to the left of the mid-line.

The right eye and right side of the face were normal. When the patient was seen again, November 27, 1929, the swelling of the lids was less, and the pre-auricular gland felt much softer than before. A smear taken from the left eye showed Kochs-Weeks bacillus, confirmed by culture.

The pre-auricular gland is to be removed and injected into a guinea-pig.

Mr. WILLIAMSON NOBLE said that the gland should be dissected out. He mentioned a case in which, on dissecting out the gland, the condition of tuberculous conjunctivitis was clearly demonstrated. He did not think one was justified in diagnosing any case of Parinaud's conjunctivitis unless one had the whole gland dealt with.

Cyst of Retina in a Boy aged 13.—HUMPHREY NEAME, F.R.C.S.

This is a case of simple detachment of the retina, in which there is a large hole. The boy was treated in hospital in the recumbent position for a fortnight, but he proved quite hopeless, as he was incapable of resting, and was finally sent out again without any trace of improvement in his condition. The large size of the hole is rather striking, and the latest method of treating such cases, namely, that of trying to seal up the hole with a cautery, would here be almost impossible. An interesting feature is the cyst of the retina just posterior to the extreme edge of the tear. If the free edge of the tear occupies one-sixth of the circumference, the cyst occupies about one-half that extent, projecting inwards into the vitreous cavity and outwards in the sub-retinal space. I merely show this case as one of a cyst of the retina of considerable size. I do not think there is any special treatment to be adopted.

Abnormal Type of Interstitial Keratitis.—HUMPHREY NEAME, F.R.C.S.

Patient, male, aged 41. Six years ago had a sudden onset of right hemiplegia and came under the care of Dr. A. M. H. Gray, who diagnosed venereal disease. The Wassermann reaction was positive. There was almost complete recovery from the paralysis, but the patient has since suffered from attacks of redness of the right eye lasting only for a day or two at a time. It is not the redness which troubles him, however, but the opacity just above the middle of the cornea. The vessels in this area of opacity are mostly superficial, though a few are fairly deep. They appear to rise from the episcleral vessels. A peculiarity about the case is the crystalline appearance of the deep surface of the cornea. A glistening appearance in this area puzzled me, but with the slit-lamp microscope it can be isolated as being concerned with the posterior surface of the cornea entirely. I presume that this is an abnormal type of interstitial keratitis.

Opaque Strands Projecting into the Retina. ? Retinitis Proliferans. ? Congenital Abnormality.—HUMPHREY NEAME, F.R.C.S.

I am showing this case in order to obtain an opinion as to opaque strands projecting into the vitreous from the retina in the temporal region of the right eye. The history is of sudden loss of sight in the right eye, with gradual recovery. The vision in this eye is now $\frac{6}{6}$, and in the left eye $\frac{6}{5}$, with correction. The strands in the right temporal region are connected with a branch of the superior temporal artery, and I am wondering whether there is the possibility of its being congenital, because of the peculiar way in which these strands pass into the vitreous and branch into numerous fibrils. The temporal half of the right disc is pale.

Miss IDA MANN said the appearances were rather in favour of the condition being inflammatory. There was no embryological reason why the strands should be connected with so peripheral a branch of the artery. One could also see a patch of what looked like choroidal disturbance close to the strands and another patch below where there were no vessels. She thought it was probably allied to retinitis proliferans.

Glioma Treated by Intra-ocular Insertion of Radium.—R. FOSTER MOORE, F.R.C.S.

For this case I have to thank Mr. Rupert Scott, who knew of my interest in the condition and transferred it to me for treatment. The patient is a boy, aged 4 years. His elder brother had had both eyes removed for glioma and had died in spite of the operation. Mr. Rupert Scott removed this patient's left eye for glioma two years ago and under these circumstances the parents refused to have the right eye removed. I therefore felt justified in treating it by means of radium.

The growth was of considerable size, its nearest point being four discs' breadth from the disc edge. I hoped I might be able to bury a radon seed completely in the

substance of the growth. I had previously practised the technique of this kind of procedure on more than two dozen eyes, as a preliminary to removing them. I was fortunate to have the assistance of Mr. H. B. Stallard, and on November 8, 1929, under general anæsthesia, the eye having been fixed in position by means of a stitch, a large flap of conjunctiva was reflected and the sclerotic exposed cleanly nearly as far as the entrance of the optic nerve. It was found possible to do this without dividing any muscle.

In order to get the line of the growth I examined it with the ophthalmoscope and asked Mr. Stallard to place a pair of closed forceps on the sclerotic outside, and to shift them a little to one or other side as was necessary, until the apex of the growth—as seen through the ophthalmoscope—and the forceps—as seen by looking immediately over it—were in a straight line.

The next question was as to how far back in the globe to make the incision. I wondered whether it would be possible to get the seed sufficiently far back. Having reached what I judged to be a suitable position, I made an incision with a narrow von Graefe's knife through the sclerotic, and taking the seed in a pair of forceps, endeavoured to slip it through the incision into the growth. My endeavour was to introduce it through a hole which was just large enough to admit of its entrance and no larger, and to this end I had several times slightly to enlarge the original incision, and it was for this reason, too, that I preferred not to use any form of introducer. The seed was now introduced, its hind end was slipped through the sclerotic, the attached black silk was cut short and the conjunctival flap replaced. On examination with the ophthalmoscope the vitreous looked perfectly clear and the whole of the inside of the eye was seen distinctly, and this is still the case.

It could now be seen that we had hit off the growth very closely. The seed was tunnelling a large part of the growth, its apex projecting towards the disc about one disc's breadth nearer the disc edge than the nearest part of the growth. There was no hæmorrhage of the vitreous, nor did this occur at any time.

Immediately after the introduction of the seed, a filmy cloud—which later became a good deal larger—was seen on its surface. It seemed likely that this was a film of coagulated vitreous.

The seed was left in for ten days, the conjunctival flap was turned back, the short end of the black silk found and the seed removed without difficulty. Again no hæmorrhage into the vitreous occurred and when seen with the ophthalmoscope the clean-cut hole through which it had been introduced looked much like a golf hole.

The growth has very largely disappeared. It cannot be said to have disappeared completely, nor would this be expected after so short an interval. I am hoping, of course, that we have completely destroyed the growth cells and I shall keep a close watch upon the case, and, at a subsequent date, report in detail the late result of the treatment. The seed was of a strength of three millicuries.

Rupture of Descemet's Membrane.—F. A. JULER, F.R.C.S.

Patient, a boy, aged 14. One eye defective since birth: history of injury by forceps during delivery. The case shows the usual features—oblique scar in cornea, high astigmatism, high degree of amblyopia. The corneal microscope, with slit lamp illumination, shows that the Descemet's membrane is floating in the anterior chamber over a certain area, being attached along one border and free at the other: these two borders come together above and below.

Siderosis of Lens Capsule.—F. A. JULER, F.R.C.S.

Patient, a boy, aged 17, came to hospital complaining of defective vision in one eye. He had not for eighteen months past been in any occupation in which he might have been injured with a flying bit of metal, but previous to that time he had been in an engineering works.

An interesting feature is that the orange-red colour of the lens opacities suggested the nature of the case, and led to the discovery of a penetrating scar of the cornea. Further, no foreign body could be discovered by X-rays, and the magnet test was negative. This suggested that a minute bit of iron had entered the eye, and had been absorbed after it had caused the rust-staining.

Miss IDA MANN said that she had seen an analogous case under Mr. A. C. Hudson—the patient had originally been under the care of Mr. Treacher Collins. There was a perfectly definite history of a foreign body, which had been demonstrated and localized by X-rays, and an attempt at extraction had failed fifteen years before. There was a history of subsequent siderosis, which had been watched for about four years by Mr. Treacher Collins. When the case was seen eventually by Mr. A. C. Hudson, about ten years later, there was no trace of siderosis and no sign of the foreign body. The patient had an aphakic eye with $\frac{6}{9}$ vision with correction. Subsequently glaucoma had developed in the eye, but she did not know whether it had any connection with the earlier condition.

Detachment of Retina.—F. A. JULER, F.R.C.S.

B. S., female, aged 30. January, 1920, myopia 12D. After three weeks' treatment in bed, by subconjunctival saline injections, etc., she was discharged without improvement. In March, 1920, the retina had become re-attached and has since remained in place. November, 1929: Peripheral pigmentation in outer half of left fundus. Left vision = J1, with difficulty. Some limitation of field.

Mr. JULER said he had intended to show a second case of the condition in a man aged 30, but the patient had not turned up. That case was important because in February, 1925, a tear had been seen in the detached retina. A sketch had been made of this hole at the time and he now exhibited the drawing. The detachment had followed a vitreous hæmorrhage. Five weeks afterwards the retina had returned into position. In March, 1929, the retina was in position throughout. Vision with glasses (- 5) was $\frac{6}{5}$; the field was full to 1 degree object (white); some contraction to 1 degree (red).

An Unusual Case of Deep Scleritis.—ADRIAN CADDY, F.R.C.S.

H. S., male, aged 31, a chauffeur. Three months ago something flew into his left eye while he was driving. Shortly afterwards the eye became red and inflamed and a swelling developed at the limbus under the upper lid.

When I examined him at the Royal Westminster Ophthalmic Hospital I found a well marked rounded swelling the size of a pea growing from the sclera and extending a little way on to the cornea; it was actually part and parcel of the sclerotic. It was considerably inflamed, the inflammation involving the whole ciliary region, and there was some effusion into Tenon's capsule giving the clinical picture of a "brawny scleritis." The fundus was healthy. The right eye was normal in every way; vision $\frac{6}{6}$.

The only point of note in his past history was that nine months previously he had exposed himself to infection and had developed a "sore" on the penis. This had disappeared after a few intravenous injections of (presumably) some arsenical compound. The Wassermann reaction was investigated and found negative.

The diagnosis appears to be one of three things: (1) Deep scleritis; (2) cystic growth at the limbus, which has become inflamed; (3) gumma.

Treatment has consisted of atropine locally and salicylates internally. If improvement is not obtained I propose to try diathermy with iodides internally, followed, possibly, by puncture of the swelling and the removal of a piece of tissue for examination.

Mr. HUMPHREY NEAME said that the swelling above the cornea seemed to be firm and solid. Although no cutaneous eruption or other secondary features had been noticed by the patient, it was probable that the condition was gummatous. The case would pass very well for one of episcleral gumma, a diagnosis not contradicted by the negative Wassermann reaction, which might be the result of the previous treatment.

POSTSCRIPT.—January 16, 1929.—The swelling has somewhat decreased in size. I have tried treatment with iodides but the patient has great difficulty in taking these and has had only two or three doses.—(A. C.)

Rodent Ulcer: Result of Operation.—M. H. WHITING, F.R.C.S.

B. D., male, aged 63. I saw this patient in October, 1928, when he stated that "inflammation" of the right side of the nose and of the right eyelids had been noticed for about eighteen months before he attended hospital.

October 29: Microscopical examination; the growth was shown to be a rodent ulcer. November 8: the ulcer was excised, the area removed extending from the centre of each eyelid to the centre of the bridge of the nose and including the lacrimal sac and all the soft tissues down to the bone in this region.

November 12: a pedicle flap was turned down from the forehead and sutured in position. November 19: the raw area on the forehead was Thiersch grafted.

January 17: plastic operations were carried out to improve the appearance of the result. These included removal of some redundant skin on the bridge of the nose and of subcutaneous tissue under the eyelid part of the flap.

The present condition shows no sign of return of the growth; the vision is $\frac{6}{9}$ and the only inconvenience is a little lacrimation in cold or windy weather.

Eales' Disease: Retinal and Vitreous Hæmorrhages.—M. H. WHITING, F.R.C.S.

F. D., aged 34. I saw this patient first in July, 1928, when he gave a history of the sight in the right eye being affected for one month. Vision in right eye: counting fingers at distance of 1 ft.; in left eye: $\frac{6}{6}$. The right eye showed extensive vitreous opacity due to hæmorrhages from the retina; the left eye appeared to be quite normal.

In spite of tuberculin treatment, the eye did not improve and in October, 1929, the left eye began to follow the same course.

The following cases were shown by Mr. J. BRUCE HAMILTON:—

(1) (For Mr. W. S. DUKE-ELDER), "Rodent ulcer on the lower eyelid in an elderly man." On account of the patient's age, radium treatment had been initiated.

(2) (For Sir WILLIAM LISTER), "Changes in the macula; ? meningeal nævus." The patient had improved greatly while she had been in hospital.

Section of Epidemiology and State Medicine.

[*January* 24, 1930.]

Industrial Efficiency and Fatigue.

By G. P. Crowden, M.Sc., L.R.C.P., M.R.C.S.

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Abstract.—The problems of industrial efficiency and fatigue offer increasing scope for the use of that special knowledge of human life with which medical men are equipped by their training. Success and prosperity of industry depend as much on health and efficiency of workers as on the efficiency of machines. Impetus given by European War to study of this human factor; national necessity led to establishment of Health of Munition Workers Committee which later developed into the Industrial Fatigue Research—now the Industrial Health Research—Board of the Medical Research Council. In Germany extensive investigations are now pursued at the Kaiser-Wilhelm Institut für Arbeitsphysiologie, at Dortmund, into such problems as relationship of age to capacity for heavy muscular work, influence of diet and nutrition on human efficiency, and optimum height of stairs up which loads have to be carried; new system of training apprentices developed in Germany since the war.

Factors influencing efficiency and capacity for work of employees may be placed in two general groups, intra-factory conditions, and extra-factory conditions. Many of these factors have been investigated in this country and in America. In particular, the effect of the environmental conditions of temperature, humidity and air-movement on human efficiency has been studied: but much remains to be done.

The subject of this paper, "Industrial Efficiency and Fatigue," may appear to be rather remote from medicine, or at least rather different from the subjects usually dealt with at meetings of the Royal Society of Medicine. I hope to show, however, that it is one with which medical science is intimately connected, and that not only in this, but also in other countries, medical men and medical scientists are finding in the human problems of industry increasing scope and demand for that special knowledge of human life with which their training equips them.

The success and prosperity of industry depend as much on the efficiency of the workers as on that of the machines. The machines can only work and maintain maximum efficiency if their pace coincides with the optimum physiological pace of the operatives for the manual and mental operations involved. It is quite conceivable that the design and pace of a machine may so cramp the operative, or force him to work at such a speed, that the efficiency which the machine gains from an engineering point of view, the factory loses in human efficiency, by sickness, lost time or increased labour turnover. Industrial efficiency is, therefore, as much a problem of physiology and preventive medicine as of engineering or organization or business management. The psychological problems of industry are also of great importance, but in many cases these arise or become acute because the physiological requirements of the workers have been lost sight of or disregarded by the workers themselves or by the management. Speaking generally, the separation of the human problems of industry into psychological and physiological compartments is unsound; both are parts of one science and the most intimate liaison must be maintained between the specialized workers in each if the maximum of service is to be rendered by medical science to the great body of industrial workers. In this country the National Institute of Industrial Psychology fortunately combines physiological and psychological methods in its investigations of problems arising in factories. This institute pays particular attention to the

questions of vocational selection and vocational guidance. The fitting of square pegs into square holes is of the utmost importance to both the workers and the factory.

The study of the efficiency and fatigue of industrial workers received the stimulus of necessity during the European War when it soon became apparent that the demands for munitions could only be met if the human machines were properly looked after, in addition to being adequately paid. The Health of Munition Workers Committee was established, and in 1916 recommended that proper organization of medical services in factories was essential not only for the health of the operatives, but in order to secure improved production and output by preventing loss of time and efficiency among the workers.

Towards the end of the war the Health of Munition Workers Committee ceased to exist, and in its place a Research Board was appointed (in July, 1918) jointly by the Medical Research Committee and the Department of Scientific and Industrial Research. This board later became established as the Industrial Fatigue Research Board of the Medical Research Council with the following terms of reference:—

"To suggest problems for investigation and to advise upon or carry out schemes of research referred to them from time to time by the Medical Research Council, undertaken to promote better knowledge of the relations of hours of labour and of other conditions of employment, including methods of work, to functions of the human body, having regard both to the preservation of health among the workers and to industrial efficiency; and to take steps to secure the coöperation of industries in the fullest practical application of the results of research work to the needs of industry."

The name has recently been changed to the Industrial Health Research Board, and in this country this is the organization which has the responsibility of placing the resources of medical science at the disposal of industry. The problems of the health, efficiency and comfort in work of the employees in industry must be seriously regarded and earnestly pursued if the prosperity and happiness of labour in England is to be secured, and if this nation is to hold its own in industrial competition with other countries.

Since the war there has been a great forward movement in Germany in the application of medical science, particularly physiology, to the problems of labour, and there are signs of an awakening in Russia, which seems to be following Germany in this direction. The organization responsible for progress in Germany is the Kaiser-Wilhelm Gesellschaft, under the auspices of which the Kaiser-Wilhelm Institut für Arbeitsphysiologie was established at Berlin. The work of this institute has for many years been directed by Professor Dr. Edgar Atzler.

A few years ago it was felt that this institute for the study of the physiology of labour should be located in the industrial area, and a competition between industrial towns was organized, with the result that early in 1929 the institute was transferred to Dortmund in Westphalia in the heart of the iron and steel industries. The industries in the vicinity of Dortmund subscribed the necessary capital, about £60,000, for the construction of the new building, which is rather like a large modern factory in appearance, and very well equipped for physiological, psychological and biochemical research. Professor Atzler has gathered round him an able and enthusiastic team of workers, medical men, physicists, engineers, psychologists and biochemists. The research work carried out there deals with such problems as human efficiency for heavy muscular work at different ages; the effect of arteriosclerosis on efficiency; the influence of nutrition and diet on efficiency; the optimum weight and frequency of stroke of hammers; the optimum position of levers and hand wheels for controlling machines; the optimum height of steps of stairs up which loads have to be carried, and other problems. One large room at the institute is devoted to the exhibition of diagrams and models for the instruction of works engineers and foremen. In this a beautifully-modelled series shows the result of a research on men drawing trucks with handles at varying heights, and

another series depicts the results of one of the researches of the Industrial Fatigue Research Board, namely, the work of Miss Bedale in Professor Cathcart's Laboratory at Glasgow, on the efficiency of women carrying loads in various ways.

The XIIIth International Physiological Congress at Boston, Mass., in August, 1929, offered a great opportunity for close contact to be established between German, American and English workers in this field: contact which, it is hoped, will lead to a continuous interchange of ideas, for in this study, as in medicine, there are no boundaries of nation or race; the problems are human problems of health and comfort.

Now to turn to the consideration of the factors which influence the working capacity or efficiency of employees—factors which influence fatigue, for fatigue may be defined as a diminution in capacity for doing work. First, perhaps, in order of importance, certainly from the point of view of efficiency in industry as a whole, comes the question of the nutrition of the workers—their standard of living. The experience of Germany during the war is of considerable interest in this connection. In the early part of the war the bread ration in Germany was reduced by cutting down the allowance of flour per head of population. English physiologists who were considering the problems of the food supply of the United Kingdom, predicted that this reduction of the bread ration in Germany would either lead to calamity or have to be discontinued, and their view was amply justified. An adequate supply of bread, above all other foodstuffs, is essential for industrial efficiency, because it forms the main source of energy for the industrial worker. Roughly speaking, compared with the middle classes, the manual worker in industry normally consumes twice as much bread per week. The consumption may be as high as 10 lb. per head per week. The average consumption per head of population is of the order of 5 lb. per week, and if a rationing order suddenly reduced this to 3 lb. per head per week without discriminating between the average and the requirements of the industrial worker, it is clear how severely the latter would be hit. The requirements of the worker vary with the muscular effort involved in his work and unless he has enough food for his basal needs as well as for his work, either he will not do so much work, or if he does, he will do so at the expense of his own tissues, and sooner or later his health will suffer and forcibly reduce his output of work. The bread supply of this nation must be liberal if industrial efficiency is to be maintained. Practically no other food is as cheap a source of energy as bread, and it must remain so.

The individual problem—as well as the general problem—of the nutrition of the industrial worker must be considered. For the ordinary physiological processes of life, muscular action of the heart, respiration, glandular activity, maintenance of body temperature, there are basal requirements of energy which cannot be avoided by anyone. In the average adult man these requirements amount to about 1,700 calories per day even though he is asleep in bed. If he is up and about although doing no work he will need at least a further 300 calories. If he does moderate muscular work he will need an additional 1,000 calories, making 3,000 calories per day the minimum requirement. Suppose now, either by rationing of food stuffs or bad household catering, the calories he receives in his food are reduced by one-fifth, so that he receives only 2,400 calories. Let us examine the effect on his capacity for doing muscular work. If he is to maintain his weight and health he will need at least 2,000 calories, which leaves 400 for the muscular work for which he requires 1,000. This means that his capacity for doing work will fall from the physiological work equivalent of 1,000 calories to that of 400, in other words, there will be a 60 per cent. diminution. From these figures it is clear how serious a matter rationing, or bad household feeding may be to the manual worker and to industry. Industrial efficiency would be helped by education of the wives of many workers in the best ways to spend the food allowance for the family.

Apart from considerations of the food requirements of the manual worker, there

are many other factors which influence his working capacity. These have been conveniently grouped by Wyatt into two general classes: intra-factory conditions, including ventilation, temperature and lighting; and extra-factory conditions, under which heading come such factors as health, housing and habits. A good deal of work has been done on many of these factors, both in this country and in America, but a great deal remains to be done before it will be possible to prescribe a code of living and working which will ensure that the worker is given full opportunity of optimum performance from the point of view both of daily production and of life production.

It would be interesting to know whether the methods of speeding-up production, which are more commonly employed in America than in this country, namely, the conveyor systems which set the pace for the worker throughout the working day, are good or bad for him from the point of view of the duration of his efficient working life. It is possible that Mr. Ford by employing a five-day week, has found a means of compensating for increased daily effort and monotony.

In regard to the intra-factory conditions of temperature and ventilation, which includes humidity and air-movement, Professor Leonard Hill has developed a method of assessing these variables in one measurement, namely, the cooling power of the air as measured by his katathermometer. Investigators of the Industrial Fatigue Research Board, Vernon and Bedford, have determined by observations in a number of factories the cooling powers agreed to be comfortable or otherwise by workers when doing sedentary work, or light, or heavy, manual work, and these standards are useful when assessing the atmospheric conditions in factories or works generally. In America a different method of assessing is adopted, namely, the "effective temperature scale." This system was largely due to the work of Mr. C. P. Yaglou, who is now working with Professors Cecil and Philip Drinker, at the Harvard School of Public Health, where problems of human efficiency at various temperatures and humidities are being studied at the present time. Such work is done in a specially constructed room in which it is possible to produce temperatures ranging from freezing to 160° Fahrenheit and almost any degree of humidity or air movement. The subjects of these experiments perform a measured amount of work on a stationary bicycle ergometer and their reactions, pulse-rate, blood-pressure, respiration, body temperature, sweating, and metabolism are determined. On the "effective temperature scale" the actual conditions of the air as regards dry and wet bulb temperature and air movement, are combined in one figure which represents the actual temperature which saturated still air would have to possess in order to produce the same sensation of comfort or discomfort in human beings. The desirable cooling power, or effective temperature, of the air varies with the nature of the occupation—a greater cooling power or lower effective temperature being recommended the heavier the work performed.

Certain American firms spend a great deal of money and effort on the health and welfare of their workers inside and outside the factories, and it pays them to do so, for it reduces the loss of time due to accident and sickness. Such care also decreases labour turnover by making the employees more contented, while careful medical examination prevents new workers being given—or old employees being allowed to continue—work for which they are unfitted. By "labour turnover" is meant the rate of change of working staff. The more skilled the work, the more serious is the loss of a worker to the factory. Mr. Ford has partially overcome this difficulty by splitting up the manufacture of his motor-cars into thousands of operations. Each operation by itself is a relatively simple affair which can be learnt in a very few minutes by a new employee, and in a very short time he can acquire sufficient skill to carry out the task within the time permitted by the conveyor belt. The loss and replacement of a worker is not such a serious matter under this system, for it costs relatively little to educate the new employee in his job. Such a system as Mr. Ford

has evolved is capable of providing a means of livelihood for a vast number of able-bodied men who possess little skill or even natural ability, while, at the same time, as a team they work very efficiently. Housing schemes, model dwellings, automobiles purchased out of wages on the instalment system, as at Ford's works—all such things tend to reduce labour turnover by making the extra-factory conditions of life easier for the workers, and comfort in the home is reflected in efficiency and contentment in the factory. The medical men attached to these factories advise on such questions, and maintain contact with the actual working conditions in the workshops in addition to treating employees when they come up to the factory hospital. Factory medical officers have to study, in particular, how time may be saved in dealing with cases. "Time is money" both to the piece-rate worker and to the works. At the Norton Engineering Works at Worcester, Mass., Dr. Irving Clark, the medical officer in charge of the Service Department, has paid particular attention to labour-saving and time-saving devices and routine. In passing, a few of these devices may be mentioned, for example, chairs with arm-rests at a convenient height for the nurse or doctor to dress hand injuries without stooping or requiring the patient to stand up; small breadboards on which strips of adhesive plaster of varying size are affixed ready for immediate application; chairs with sliding leg-rests which can be drawn out when necessary, and other devices which would probably be of use and save time in the crowded casualty departments of some of our London hospitals. In addition to maintaining efficient medical service in the factory, some of these whole-time factory doctors are pursuing research into the incidence of sickness, and on the early signs of disease. They have unique opportunities for such investigations, as they deal with relatively stable populations of several thousand persons always under observation. At some works, such as those of the General Electric Company at Lynn, near Boston, individuals with special training and ability are occupied solely in studying the employees at their work and seeing how fatigue can be reduced; for example, by enabling them to adopt a comfortable posture at the work bench or improving the illumination of their work. In regard to visual fatigue, a very interesting and useful investigation was recently carried out by Weston and Adams for the Industrial Fatigue Research Board. The occupation studied was that of linking in the hosiery industry. They showed that the efficiency of the workers could be improved and fatigue lessened by the use of suitable glasses.

In regard to problems of heavy muscular work, it must be fully recognized that the actual amount of energy expended is not in itself a measure of the fatigue which will be produced. The way the energy is expended, whether it is used in static or dynamic effort, must be taken into account. It is, however, true to say that the onset of fatigue is delayed if the work is so arranged that with the expenditure of minimum energy the maximum performance is produced. The expenditure of energy of the worker for doing work in various ways or at varying rates can be measured, and it is therefore possible to determine the most economical method of working from the point of view of energy consumption. This is done by measuring the oxygen consumption of the worker at rest and during an equal period of time at work, the difference being the oxygen cost of the work which is directly proportional to the energy expenditure of the individual for the work performed. The method used in this country is that of the Douglas bag and the Haldane gas analysis apparatus. This method has been used by Professor A. V. Hill in the investigation of many problems of human muscular effort, and can be readily employed in the study of the types of labour common in industry as, for example, carrying loads, wheeling barrows, or lifting weights.

There are, of course, many other aspects of industrial health, efficiency and fatigue which are of great importance, as, for example, the seasonal occurrence of epidemics or the special industrial hazards due to poisonous fumes and dusts, but with these I have not attempted to deal.

There are, however, two subjects in particular which I should like to mention very briefly. One is the question of the length of the working day, the other is the training of apprentices for industry. Both are factors which profoundly affect industrial prosperity through the influence which comfort and health in body and contentment in mind have on the workers' efficiency and will to work.

In regard to the first subject—the length of the working day—this problem became acute during the war, and, on behalf of the Health of Munition Workers' Committee, Dr. H. M. Vernon carried out an investigation in a factory where women were employed turning fuse bodies. He found that, with a seven-day week, comprising sixty-six actual working hours, the hourly output averaged 108 fuse bodies. When this was reduced to a 54·4 working hours per week, the hourly output rose to 131, while the total output per week remained practically unchanged. When, however, Sunday labour was abolished, and the actual working hours were reduced to 47·5, the hourly output rose to 169, and the total output increased to 13% above the level of that in the seven-day week. As long ago as 1893, the firm of Messrs. Mather and Platt of Manchester showed that a reduction from fifty-four to forty-eight hours per week caused an increase in production and a decrease in lost time. It appears, therefore, that there is considerable justification for the advocacy of a forty-eight-hour week. Complete recovery after work is an essential requirement if the worker is to maintain his efficiency and health, and opportunity for this should be provided by the week-end break.

In regard to the second subject, namely, training for industry, a very common method of training apprentices is to draft them into the factory or engineering shop and place them under the guidance of a foreman or worker. In the evenings they are expected to attend classes at a technical school. The success of this system is rather a matter of chance. Since the post-war industrial crisis in Germany there has developed a new system of training apprentices for industry, the "Deutsches Institut für technische Arbeitsschulung," known, for short, as "Dinta." This organization was started at Düsseldorf at the suggestion of an ex-officer of the Imperial German General Staff, Herr Arnhold, who insisted that interest and pride in work in the spirit of the ancient guilds must be cultivated and developed in industry if calamity was to be averted and industrial prosperity restored to Germany. He said that this could be achieved by reorganizing the system of training of apprentices for industry. Last July I had the opportunity of seeing the "Dinta" system at work at a large steel works at Gelsenkirchen, near Essen. The apprentices under this system, boys of from 15 to 18 years of age, are not trained in the main works. They are drafted into self-contained little factories, each representing some section of the main works. They become shareholders in these little factories from their day of entry. They assess their progress towards efficiency by means of a system of cards. A card is given to them for each particular job and on it they record the time taken to complete the work. On the card is printed the time taken by a skilled worker for the same piece of work. The apprentice can see from day to day how he is progressing towards efficiency, and he can follow the part he is playing in the success of his particular little factory, for, each week, curves of output and turnover are posted. During their three years' course the apprentices pass, in miniature, through all the departments which make up the main works—mechanical shops, storekeeping, book-keeping, so that they acquire an understanding of the works as a whole, and, without question, they develop an interest in their work. The boys in the foundry at the steel works at Gelsenkirchen were like boy scouts round their camp fires. "Dinta" is in close touch with the institute at Dortmund, where problems of the physiology of labour are being investigated. This close liaison between medical science and industry proper, coupled with the spirit of "Dinta," is full of promise for future comfort, efficiency and happiness among the industrial workers and for industrial prosperity.

I hope I have been able to show that there is ample scope for the application of medical science to the human problems of industry, and I feel sure that in this direction there lies a vast field of useful work to be done and of opportunities of service to the workers on whom the prosperity of a nation ultimately depends.

Discussion.—Professor M. GREENWOOD (communicated): I am glad to say that the prospects of advancing knowledge seem brighter than they have been for some time. Not only has the experience of the Industrial Fatigue Research Board supplied a basis of judgment as to the lines of inquiry likely to be profitable, but the opening of the London School of Hygiene and Tropical Medicine will enable us to offer facilities on the educational side which have hitherto been lacking. I have been officially connected with the work of the Industrial Health Board since its foundation, and one of the difficulties of the Board has always been the provision of academic instruction. First we were ignorant of the kind of instruction required and now we know that a sound training in the physiological principles and an intelligent grasp of the element of statistical methods are indispensable. But beyond that, it is increasingly borne in upon us that insight into what for lack of a better term I may call clinical psychology is a very important desideratum. I am becoming more and more convinced that an effective investigation of the major problems can only be made by young medically qualified persons who have had a special course of instruction.

I fear that Dr. Crowden may be a little too optimistic in the half-suggestion that a considerable proportion of the psychological problem of industry is secondary to the physiological problem. My own experience, which is now a fairly wide one, of the factors of lost time and minor incapacity in industrial establishments, leads me to put much more weight upon the psychological than the purely physiological elements. One of our difficulties as medical men in approaching psychological problems has been that during the last decade clinical psychology was a battle-ground of infuriated partisans, each satisfied that his piece of truth was the whole truth. This phase is passing away, and it has become possible to give academic instruction free from the particularism of sects. It was right and proper that at the beginning of investigation predominant importance should have been assigned to physiological methods. Now, however, emphasis should be given to the psychological side, without of course impeding the development of physiological work. There is certainly a danger of tempting young men and women, who have had no medical training, into this most difficult branch of investigation or, on the other hand, of allowing medical men and women to suppose that medical psychology is easy and that the perfunctory instruction which they may have received as undergraduates is sufficient for their needs.

The PRESIDENT (Colonel F. E. FREMANTLE) said that Dr. Crowden's paper represented the scientific measure of rationalization of industry. But in his investigation allowance had not been made for the factors of food, drink and clothing, factors known to be of first importance in athletics. Henderson Hunt, the physiologist, imbibed 8½ gallons of water during a day's shooting through the jhils—a most severe form of exercise, in tropical heat. In contrast with his companions, who followed the tradition of not drinking, and were too much fatigued to continue in the afternoon, Mr. Hunt and a friend, drinking water freely, went on without any feeling of exhaustion to the end of the day. In Mesopotamia during the late War, the free drinking of cold water was encouraged, with consequent reduction of the incidence of heat-stroke, and increase of efficiency. The use of the katathermometer should be general; records of temperature or moisture alone were of little value. "Rate of cooling" depended also on the clothing; for without appropriate clothing, the air could have little cooling power. The human sentient body was the bestefficiency-testing machine, but scientific analysis of factors of efficiency was invaluable in the training of workers and foremen, and for the improvement of factory arrangements and guidance in administration and legislation. The Diploma of Public Health should be developed to include industrial medicine, and applied physiology should be taught to medical students. Crude statements as to efficiency of length of working day were of little value without relation to the nature of the work done.

Sir ANDREW BALFOUR outlined the part which the London School of Hygiene and Tropical Medicine hoped to play in teaching and research with respect to the problems of public health as related to industrial psychology.

Dr. N. HOWARD MUMMERY said that whilst reference was constantly made to work going on in America or Germany, too little interest was taken in the equally valuable work being done by medical practitioners associated with industrial factories in England, a

considerable number of whom for some years past had been discussing these problems in the Council of Industrial Medicine now intimately associated with the Industrial Welfare Society. Deductions from experiments on diet, rest pauses, etc., though excellent in the abstract, often proved impracticable on application in a busy factory. Progress in the management of the human element in industry was most successfully attained by education and example; drastic alterations were not welcomed by managers and did not promote output. Labour turnover was an extremely interesting aspect of the problem, but though its estimation was comparatively easy with a relatively stable factory population, it was very far from being easy when seasonal variations necessitated the temporary employment of large numbers of employees. Vocational selection in some degree was essential in a modern factory, and medical examination for the particular job proposed proved of the utmost value to the employer. The extra-factory conditions of employees, except in model factory villages, were largely governed by housing difficulties, and by the limitation of benefits, medical services and nursing under the National Health Insurance system, but much was being done in this direction by the sick visitor following up the employee in his home and by the provision of factory medical services and facilities for obtaining expert advice and convalescence.

With regard to visual fatigue: Cylindrical plus spectacles appeared to assist emmetropic eyes when the work involved fixing the vision on one object, but the provision of such glasses was harmful when the work was concerned with several objects between which the eyes had to move. As an example of the efficiency of the trained manual worker and the skill that could be developed in certain processes, he might mention the occupation of making butter pats. In the factory with which he was concerned these were made by hand and, so far, no machine had been invented which could compete with manual labour at this work. The most skilful girl in the factory made 15,680 pats of butter in a working day of seven and a half hours; this represented 2,091 pats per hour. A machine for this work, which was at present under test, took, on an average, twenty-three minutes to make 640 pats, whereas by hand that number could be turned out in eighteen and a half minutes.

The conveyor system was, of course, largely used in factories, and provided its speed was adjusted to the capabilities of the average worker it should not involve any hardship, but rather prove a convenience. The Bedaux system was increasingly used in this country and from the medical point of view needed careful watching, as it was liable to cause the employee to work at the top of his bent throughout the hours of his employment.

Dr. J. D. ROLLESTON regretted that Dr. Crowden had not dealt with one important factor which influenced the efficiency of the worker, namely, alcohol. In former times beer drinking among the workers used to be permitted in the belief that it encouraged alacrity and contentment, but careful physiological experiments had shown that prolonged use of alcohol in any form, even in small amounts, diminished efficiency, especially in work requiring any skill.

Dr. CROWDEN (in reply) said that with regard to clothing it had been found necessary to make two distinct effective temperature scales, one for normally clothed individuals and one for workers stripped to the waist.

The intake of fluid by individual workers under conditions of great heat had not been taken into account when assessing the effect of various cooling powers of the air on efficiency, but the question of the water requirements of such workers was investigated by Professor Haldane, who recommended the drinking of dilute salt solution to make up for the fluid and sodium chloride lost in the sweat. He agreed that the workers would decide for themselves for or against a method of working according to their own personal sensations. The best we could do was to give the learners—the apprentices to industry—opportunities of trying for themselves methods which appear to be best from the physiological and psychological points of view. He agreed that the optimum length of the working day was influenced by the nature and conditions of the work. It was easier to work in the open air setting one's own pace than it was in a factory where temperature and ventilation were an additional strain and where the pace of working was set by the machines. He knew that in many factories close attention was given to the welfare of the workers inside and outside the factory, but in his paper he had rather avoided home conditions and dealt with certain aspects of industrial efficiency and fatigue which might, to a certain extent, be new information.

With reference to the question of alcohol, in relation to industrial efficiency, he was convinced that for the average individual worker and for industry prohibition had been a good thing in America.

Section of Electro-Therapeutics.

[*November* 15, 1929.]

Massive Collapse of the Lungs.

By Jessie E. Sheret, M.B., D.M.R.E.

When we began to investigate the cause of the slight increase in temperature and the marked increase in pulse-rate which sometimes follow operations, particularly abdominal operations, we had no idea that the incidence of post-operative massive collapse would prove to be so high, and the incidence of true pneumonia to be practically negligible.

The pulse and temperature charts of all post-operative patients were noted, but in none other than abdominal cases was there any evidence of massive collapse having occurred.

The term "massive collapse" is used in the active sense, i.e., of collapse due to the blockage of the bronchus, and the subsequent absorption of air by the blood circulating in the capillaries, rather than in the passive sense, i.e., of collapse due to pressure such as occurs in effusions.

During the investigations carried out at Ancoats Hospital the convalescence of 261 patients, 149 males and 112 females, was followed. Of the 149 male patients 18·1% showed pulmonary collapse; 51 operations through upper paramedian incisions, 29·3%; 40 gridiron incisions, 17·3%; 51 hernia and lower abdominal incisions, 6%. Of the 112 females, 13·7% showed lung involvement; 35 upper abdominal operations, 17·1%; 42 gridiron incisions, 4·7%; 21 hernia and lower abdominal incisions, 0%; 7 nephrectomies and nephrotomies, 14·3%.

Although the physical signs of massive collapse are characteristic, the most striking manifestation is shown in the X-ray examination, particularly when the collapse affects the whole of one lung. The shadow cast by the airless lung is as dense as that cast by a thick layer of fluid, and may even obscure the rib outline. The cardiac, mediastinal, and tracheal shadows are displaced to the affected side, the diaphragm is raised and the ribs fall together, assuming a tiled appearance.

When the lower lobe is alone involved, the shadow is as dense as that of the heart, and on the left side the heart may almost entirely obscure the collapsed and airless lobe. Bearing this in mind, careful observation of the position of the inter-lobar septum should be made, for, as pointed out by Dr. Twining, it is of more importance than mediastinal displacement.

Frequently the first indication of a collapse is a mottled appearance of the lung developing within twenty-four hours after operation. This nearly always occurs in the lower lobes of one or both sides, and is due to the blockage of the smaller bronchi. Lobular collapse may rapidly clear, or the collapsed areas coalesce to form massive collapse.

When the lung is again aerated, it frequently does not return at once to its normal volume.

There is no generally accepted theory as to the causation of massive collapse. Every factor which could possibly bring about deflation of the lungs has been evoked. Among these are the following:—

(1) *Compression by Paralysis of the Corresponding Diaphragm.*—Pasteur described collapse occurring in cases of diphtheria, with paralysis of the diaphragm. He described twenty-eight cases of diaphragmatic involvement, fifteen of which had a fatal issue, and in eight of these post-mortem examinations were performed. Five of these cases showed evidence of paralysis of the diaphragm for several days before death, and it was found post mortem that there was complete collapse of the right lower lobe. Of the remaining three cases, there were two in which there was collapse of the lower lobe, but no paralysis of the diaphragm, and in the third the paralysis had cleared twenty-four hours before death.

The result of these post-mortem examinations somewhat weakens Pasteur's theory.

Further doubt is cast on this explanation of the cause of collapse by the work of Jackson, Lee, and Scott, who have reported cases of diphtheria in which collapse has occurred, due to the blockage of a bronchus with membrane, and aeration of the lung has again occurred on removal of the membrane by bronchoscopy.

Furthermore, several workers, whilst endeavouring to confirm Pasteur's theory, have been unable to do so. Elliott and Dingley performed phrenicotomies in cats and rabbits, after which no pulmonary changes were noted. In cats they performed hemi-section of the cord at the level of the second and third cervical segment; complete paralysis of the intercostals and diaphragm resulted, but when the animals were killed three days later, no pulmonary collapse was found post mortem.

It would seem, then, that the theory of compression by paralysis of the diaphragm, suggested by Pasteur, has been disproved by succeeding workers.

Moreover, massive collapse is not a frequent sequel to phrenic evulsion performed for therapeutic purposes.

(2) *Spastic Contraction of the Bronchial Muscle.*—Barthels in 1861 drew attention to the occlusion of the bronchi through spastic contraction. Sante also believes that there is some reflex mechanism which produces obstruction, directly or secondarily, by secretion.

There are two main objections to this theory. In the first place, drugs such as atropine, epinephrine, extracts of lobelia, and nicotine, which normally abolish contraction of the bronchial muscle, have no effect on massive collapse, and secondly, spastic contraction of the muscles produces emphysema, and not collapse.

(3) *Angioneurotic Œdema.*—That this condition is not a cause of massive collapse of the lung seems to be established by the evidence from post-mortem examination of animals dying from anaphylactic shock. Angioneurotic œdema definitely occurs in such cases, but massive collapse has never been found post mortem.

(4) *Incomplete Block of a Bronchus.*—When a bronchus is partially obstructed but air can both enter and leave, nothing occurs. This condition forms the so-called "pass valve" type of Chevalier Jackson.

When ingress—but not egress—is allowed, emphysema, not collapse, results. This is the so-called "check valve" type.

(5) *Complete Block of a Bronchus and subsequent Absorption of the Air by the Blood circulating in the Capillaries.*—Lichtheim, in 1879, performed some remarkable experiments on rabbits. Occluding the bronchi with sticks of laminaria, he not only demonstrated that collapse occurred in the lung supplied by the blocked bronchus, but proved that carbon dioxide was completely absorbed in from ten to thirty minutes, oxygen in forty-five minutes, and nitrogen at the end of twenty-four hours

That these component gases of the air locked in the collapsing area of the lung should be absorbed according to the physiological law of Henry ("the absorption of gases into the blood varies with their pressure, the temperature remaining constant") is a fact confirming Lichtheims theory, especially as the times correspond so closely with the actual percentage by volume of the gases as measured by Pflüger, who, analysing the arterial blood of dogs, obtained the following results per cent. by volume: carbon dioxide 34·4, oxygen 22·6, and nitrogen 1·8.

Corrylos and Birnbaum in recent experimental work in which they occluded the bronchus with inflated rubber bags, again proved Lichtheim's theory to be correct.

The aeration of a previously atelectatic lung following the removal of a foreign body or a plug of mucus, has been repeatedly demonstrated by Chevalier Jackson.

Conversely, Manges uses the presence of atelectasis to localize the position of a non-opaque foreign body.

In post-operative cases there are several predisposing causes for collapse.

First among these is the hypersecretion caused by the anæsthetic, or caused by the cardiac or pulmonary condition which excluded a general anæsthetic. This hypersecretion is more marked in males than in females, possibly owing to the irritation caused by smoking.

Secondly the position in which abdominal patients are usually nursed tends to cause gravitation of the secretion into the bronchi of the lower lobes.

Thirdly there is interference with the expulsive mechanism, either voluntarily, by the suppression of cough or, therapeutically, by the excessive use of morphia.

In this series we tried to reduce the incidence by postural drainage, patients immediately after operation being placed in the reverse Fowler's position, pillows removed, and the foot of the bed elevated 20 in. Where this was impracticable, the administration of morphia was restricted.

When established, the blockage can sometimes be removed by rolling the patient on to the unaffected side and making him cough, but this does not always seem justifiable in the early stages in which it would be most efficacious.

Bronchoscopy and the removal of the obstructing plug of mucus result in the aeration of a previously atelectatic lung. This of course must be done without an anæsthetic.

Summary.—(1) Post-operative massive collapse or atelectasis is a relatively frequent sequel to abdominal operations and is due to a blocked bronchus.

(2) The skiagram may at first show a mottled appearance due to the blockage of the smaller bronchi.

(3) When the whole lung is involved, there is a complete opacity with the heart and mediastinum displaced to the affected side, the diaphragm raised and the ribs tiled.

(4) Prognosis is usually favourable, but infection is liable to occur if the collapse is allowed to remain more than seventy-two hours.

(5) Post-operative pneumonia is a rare complication, there being only one case in this series.

TWO ILLUSTRATIVE CASES (SEE FIGS. 1 to 8).

I.—B. H., aged 13. Operation: Appendicectomy. The day following the operation the patient had a typical collapse attack. He was turned on to the unaffected side but was afraid to cough. The following day X-ray examination showed massive collapse involving the mid and lower lobes right side. Two days later collapse involved the mid and lower lobe, the upper lobe now showed mottled collapse (fig. 1). Two days later the whole of the right lung showed massive collapse (fig. 2). Five days later upper lobe and periphery of mid and lower lobes show air in the alveoli (fig. 3). Seven days later upper lobe completely aerated, mid lobe still opaque (fig. 4). Ten days after this right side aerated, mid lobe shrunken and heart still displaced to the right (fig. 5).

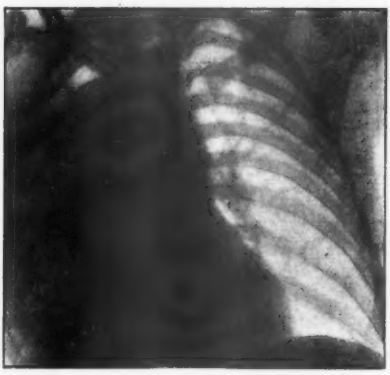


FIG. 1.—20.2.28.

FIG. 2.—22.2.28.

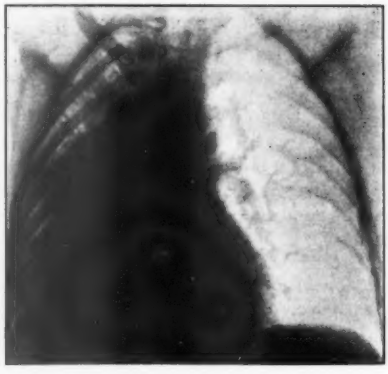


FIG. 3.—27.2.28.

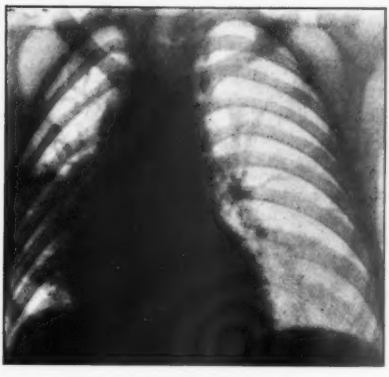


FIG. 4.—5.3.28.

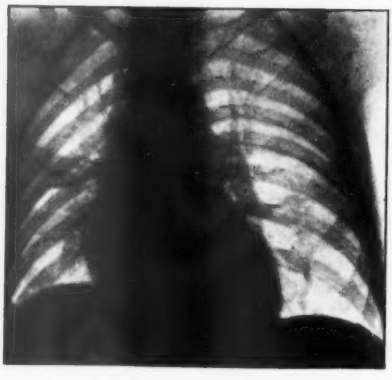


FIG. 5.—15.3.28

FIGS. 1 to 5.—Massive collapse after appendicectomy.

II.—J. C., aged 23. Operation: suture of perforated gastric ulcer. Two days after the operation right lower lobe showed mottled collapse, complete collapse of the left lower lobe (fig. 6). The following day right lower lobe collapsed, left lower lobe collapsed (fig. 7). Ten days later, right lower lobe appeared to be normal, left lower lobe still opaque (fig. 8).

FIG. 6.—30.3.28.

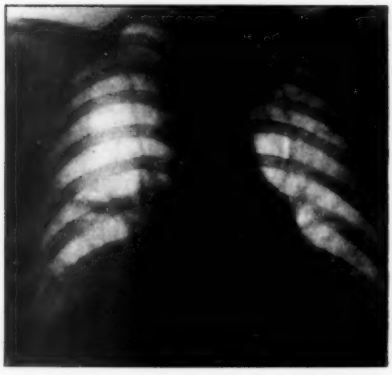


FIG. 7.—31.3.28.

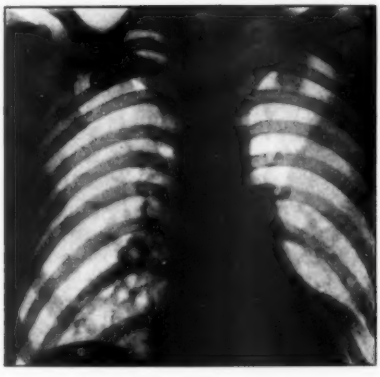


FIG. 8.—10.4.28.

FIGS. 6 to 8.—Massive collapse after suture of gastric ulcer.

Discussion.—Dr. STANLEY MELVILLE said that all radiologists were aware of the massive collapse which took place in the lobule or lobe of a lung when the supplying bronchus had been stenosed by a primary bronchial neoplasm. Collapse at the site of the lower left lobe in cases of perforating gastric ulcer had been first demonstrated to him (the speaker) by Dr. Ogle of St. George's Hospital. Among the large number of phrenic avulsions which he had seen he had never come across a massive collapse following this procedure. He thought that the reason why massive collapse was not more frequently met with was that in most cases it was of short duration and was not particularly looked for.

[Dr. Melville then drew attention to the work of Jacobaeus on the subject of massive

collapse of the lung after hæmoptysis and after the intratracheal injection of lipiodol, and showed slides illustrating a case of the first of these conditions.]

Mr. KENNETH HERITAGE said that he had had the opportunity of observing from the surgical aspect many of Dr. Sheret's cases of post-operative collapse, and had used the method of prophylaxis described, as an important part of the immediate post-operative care after non-acute abdominal surgery. The syndrome of the "collapse attack" was, as Dr. Sheret had shown, only too frequently seen in men after operations such as gastro-enterostomy or partial gastrectomy, the patient usually being labelled as "somewhat chesty." This condition, although not fatal, was responsible for a considerable degree of the ill-health and delayed convalescence after these operations. Using the method of "postural drainage" as a routine in suitable cases, the absence of the typical rise in pulse and temperature, and the freedom from respiratory embarrassment had been noteworthy—no case of pulmonary collapse having been observed clinically in cases submitted to the preventive measures.

Section of the History of Medicine.

[*December* 4, 1929.]

Book-plates of Medical Men.

By GEORGE C. PEACHEY.

A BOOK-PLATE is a label, printed or engraved, heraldic or otherwise, which is intended to proclaim the ownership of a book when pasted inside its covers or upon its flyleaves. The first book-plates, equally with the first printed books, came from Germany, and it is reasonable to suppose that their use originated in that country. The earliest plate known is the Igler plate, to which the date of 1450 has been assigned. It is a woodcut representation of a hedgehog, with a punning motto upon the owner's name, "Jean Knabensberg otherwise Igler" who was chaplain to the family of Schönstett. A copy of this was offered for sale some years age by a Munich bookseller, for £30, the largest price ever asked for a single book-plate. With two other German gift plates to the Carthusian monastery of Buxheim, these are the only book-plates of the fifteenth century, but in the new century, as printed books became more numerous and borrowing more easy, a record of ownership became necessary. The earliest sixteenth century examples are from designs of the celebrated Albert Dürer, the first of which carries the legend *Liber Bilibaldi Pirckheimer, Sibi et amicis.* Evidently book borrowing had become fashionable. It is a woodcut and carries the arms of the owner and his wife on two shields (*accolés*), his arms being a birch tree in canting allusion to his name. It dates from about 1503. For his friend and fellow-townsman, Pirckheimer, Dürer engraved a second plate bearing his portrait. And, although Pirckheimer was a jurist and not a physician, the plate possesses special interest. His library passed into the hands of Thomas, Earl of Arundel, patron of William Harvey, probably by his means. The books were eventually donated to the Royal Society, and some of them, in comparatively modern times, found their way, as duplicates, into the market. Inside the front cover of each was pasted the armorial woodcut of the one-time owner, and on the end leaf of same was impressed the portrait plate from the original copper. The copy from which the lantern slide is taken was found on the verso of an end leaf and is in my possession. It is dated 1524, is signed by Dürer, and bears the upright fractures which are mentioned as a test by Bartsch.

In the British Museum may be seen a volume, once the property of Cardinal Wolsey, and later that of his Royal Master, to which is attached the gorgeous, hand-painted armorial achievement designed for the Cardinal in the days of his power. Though not, strictly speaking, a book-plate proper, since it is neither printed nor engraved, in point of historical interest and of its association with its owner, it stands paramount and alone among English Ex Libris. The shield rests upon a platform of gold, on which are pillars supporting a canopy ornamented with Tudor roses; above the shield is the hat of a Cardinal to which rank Wolsey was elevated in 1514, and above that is the Holy Dove. The supporters are griffins. Look upon the picture before you, remember to what height of power and of opulence he attained, and then go back to his origin—he was the son of an Ipswich butcher. The absence of motto might appropriately be rectified by the addition below of the words "Splendide Mendax" which has wittily been translated by old Nares as "lying in state." But, in spite of his humble birth, in spite of the accusations against his moral character which have been so freely and, it must be admitted, so truthfully levelled against him, Wolsey stands out as the man by whose advice and recommendation Henry VIII was moved to the establishment of the Royal College

of Physicians of London, with the incorporation of which in 1518 the true history of medical education in England begins. And as such, his book-plate must possess a superlative interest to every student of the history of medicine and of the medical profession.

Apart from Wolsey's, only three English book-plates of the sixteenth century are known—Sir Nicholas Bacon, the father of Francis, Lord Verulam, dated 1574, to commemorate his gift of books to the University of Cambridge; Sir Thomas Tresham and Joseph Holand, each dated 1585.

With the advent of the seventeenth century book-plates became more numerous. They are designed in one typical heraldic style, the Early Armorial, which is to be found not in book-plates alone but in every armorial achievement; the main characteristics of which, taken as a whole, are a plain symmetrical shield, surmounted by helmet, mantling, wreath and crest. Time was when a coat of arms had a better chance of being recognized and read than an inscription, and consequently one finds that the earliest book-plates are almost always heraldic and often anonymous. Their presence was the mark of ownership. Then books were comparatively few and their value great; the book-plate was a precaution against loss. Heraldry in those days was common knowledge, but as that knowledge declined and letters became better known, they began to be inscribed with the owner's name. After a time anonymous plates became the exception, and designs other than armorial came into fashion.

The earliest medical book-plate known is a label recording the gift of books to St. John's College, Cambridge, in 1634, by Dr. John Collins, Regius Professor of Physic in that University. Claim has been put forward for this distinction by the owner of a plain label inscribed "Doctor Richard Burie An. Dom. 1622." But there is no evidence that this is a book-plate, or was ever used as such. Moreover, no other copy has been found.

The Restoration, bringing with it a revival of letters and literary taste, seems to have favoured the use of book-plates the number of which increases considerably after this date, until, at the end of the century, a sudden impulse seems to have dictated the fashion, not only of using a book-plate, but of inscribing it with a date. The heavy mantling, symbolic of the periwig of the period, appears in several medical plates of a somewhat later date, notably that of Thomas Fuller, M.D., of Sevenoaks (about 1705) whose arms—barry of six, arg. and gu., a canton of the last, are supposed to represent the iron bars which were forged by his Sussex ancestors engaged in the iron industry at the smelting works at Brightling. Another, in similar heraldic style, but of even later date, is the plate of Alexander Cuninghame, M.D., whose arms, a shakefork, represent the family tradition that an ancestor was sheltered from his enemies by being covered with hay, thus eluding his pursuers. With the opening of the 18th century the style of heraldic decoration changed and instead of massive mantling, helmet and crest, the shield was placed upon a background or frame, the interval between them being damasked or lined with fish-scales, trellis or diaper. This style has beeen mis-called Jacobean; but is best remembered as contemporary with the reigns of Anne and George I. In its principal features it bears a close resemblance to the work of Grinling Gibbons and its principal ornament is the escallop shell, which under Chippendale's treatment became the shelly border, combined with curly endive leaves. Whereas the Jacobean shield is studiously symmetrical, Chippendale, adopting the new French style (about 1730-40), carefully avoided all straight lines, using the shelly rococo border and the unsymmetrical shield leading, in the decadence of the style, to the introduction of cupids, dragons and floral sprays. From this decadence (1760-70) came a reaction to the spade or urn-shaped shield of Sheraton, Adam and Chambers, with their wreaths and ribbons, wallpins and festoons. Following this came the charming little land and sea scapes of Thomas Bewick, usually introducing an

armorial urn-shaped shield leaning against a weeping willow or a blasted tree until, with the opening of the nineteenth century, a return was made to the square-sided, symmetrical shield of earlier days. A later Victorian style arose from the designs of Sherborn and Eve, whose work, still sought for, has never been surpassed in the history of the engraver's art.

The other medical plates shown upon the screen have been chosen to demonstrate my postulate that, apart from the historical interest to be derived from the changing styles of heraldic decoration, seen as well in furniture and in architecture as in book-plates, is the symbolism of heraldry, and above all the personal equation in almost every book-plate. Not once, but on many occasions, in my biographical studies, has a book-plate afforded me the information of a marriage sought for elsewhere in vain. An impalement or an escutcheon of pretence has enabled me to strike a clue in the drafting of a pedigree which has baffled every other means of genealogical search.

Among other plates shown are those of William Oliver, M.D., the reputed inventor of Bath Oliver biscuits; of Charles Lucas, M.D., the Irish patriot; of John Walford, Matthew Turner, Robert Watson, and John Douglas, depicting various surgical instruments; of Sir John Hill, M.D., the playwright-physician, the friend and in turn the enemy of Garrick; of Erasmus Darwin, M.D., the grandfather of Charles Darwin; of Benjamin Bates, M.D., the last of the Medmenham Monks and the associate of Dashwood and Wilkes in the orgies of the Hell-fire Club; of John Coakley Lettsom; of James Currie, M.D., the biographer of Burns; of John Elliotson, M.D., one-time physician to the North London (University College) Hospital; of Sir Henry Halford, the "eel-backed baronet" of the "Intercepted Letters"; and the reputed plate of Anne, the widow of John Hunter. But strange it is that many of the masters of medicine, bibliophiles and others, made no use of a book-plate. Since I have specialized in collecting the book-plates of medical men for almost forty years, and during that period have handled tens of thousands of plates, I have been forced to the conclusion that neither Mayerne, Harvey, Glisson nor Sydenham; neither Garth, Radcliffe, Mead, Freind nor Sloane; neither Askew, Arbuthnot, Akenside nor Goldsmith; neither William nor John Hunter, Matthew Baillie nor Edward Jenner; nor, last but not least, Francis Adams, of Banchory, used a book-plate. "'Tis true 'tis pity; and pity 'tis 'tis true."

[*February* 5, 1930.]

Spallanzani on Spontaneous Generation and Digestion.

By F. Prescott.

Life and Works of Spallanzani.

Lazaro Spallanzani, perhaps the most versatile physiologist of the eighteenth century, was born on the 10th of January 1729 at Scandiano in the North Italian province of Emilia. His father, a successful advocate, personally supervised his son's early education. At the age of 15, Spallanzani went to study at the Jesuit college at Reggio di Modena, where he so impressed his teachers that they desired him to become a teacher at the college. But his father had the law in view for him. Spallanzani accordingly went to the University of Bologna to study under Bianconi and Laura Bassi, who was professor of mathematics in the University. This celebrated woman, a cousin of Spallanzani, undoubtedly stimulated the young Italian's interest in science and mathematics.

Antonio Vallisneri, a professor at Padua, induced Spallanzani's father to allow his son to study natural science instead of law. He took orders as a means of

preferment and eventually attained to the titular position of Abbé, although it is certain that all of his energies were devoted to learning rather than to clerical duties.

In 1754 Spallanzani occupied successively the chairs of logic, metaphysics and Greek in the University of Reggio in Lombardy. He held a position there until 1760, when he was transferred to the chair of natural history at Modena. Here his leisure hours were spent in research. Spallanzani soon won fame as a lucid teacher. Once his position was assured, many universities desired him to accept their chairs. In 1769 we find him professor of natural history and director of the museum at Pavia, where he had been invited by Maria Theresa, who had re-established Pavia university in 1768. It was during the tenure of this professorship that he conducted his well-known journeys, which enabled him to augment the collections of the Pavia Museum.

Spallanzani was an indefatigable traveller. He traversed Switzerland in 1779, and two years later explored the shores of the Mediterranean. During 1782 and 1783 he visited Istria and the Adriatic coast. In 1785 he was at Constantinople, Corfu and Cyprus. In 1788 he made a study of Vesuvius and the volcanoes of the Lipari Islands, as well as a complete geological and geographical survey of Sicily. The results of his exploration of the latter were published as: *Viaggi alle due Sicilie ed in alcune parti dell'Appennino* (Pavia, 1792-7). Returning to Pavia after his expedition to Sicily, Spallanzani settled down again to his university work and to further research. This was terminated by a sudden fatal seizure of apoplexy on the 11th of February, 1799.

His works are most conveniently studied in the collected edition of his works (6 vols., Milan, 1825-6). Although much eulogized, his writings have not attracted the attention they deserve. A few isolated works have been translated into French and English. In 1777 Senebier translated into French[1] Spallanzani's *Opuscoli di fisica animale e vegetabile* (Modena, 1776), and in 1784 the *Dissertazioni di fisica animale e vegetabile* (Modena, 1780, 2 vols.). There are also French[2] and English[3] translations of his *Viaggi alle due Sicilie ed in alcune parti dell'Appennino* (Pavia, 1792-1797), and a French[4] and English (London, 1804) version by Senebier of his posthumous work on respiration, *Memoria sulla respirazione* (Milan, 1803). Spallanzani's excellent work on digestion has been rendered into both English and French. His letters do not seem to have been published in a collected form.

As a teacher, expositor and controversialist, Spallanzani had no equal in his day. Though his fame rests chiefly on his physiological work, he was extremely versatile, directing his researches into the realms of natural history, geology, meteorology, embryology, physiology and topography. His investigations remain a monument of industry, diligence, and judicious criticism. As a critic he was modest, always courteous and almost apologetic. The strictures of John Hunter the English surgeon and anatomist were quite unjust. Spallanzani's experiments on regeneration in animals also drew the petulant censure of Voltaire, who heaped his usual sarcasm and ridicule upon his victim. Further attacks were made on Spallanzani by the Abbé Cotte, a well-known meteorologist of the time, and by Bomare, the compiler of the *Dictionnaire d'histoire naturelle.* Several of Spallanzani's countrymen, who were apparently jealous of his position at Pavia, trumped up a false charge of mismanagement of the Pavia Museum, but inquiry showed the accusation unfounded.

1 *Opuscules de physique, animale et végétale.* Geneva, 1777.

2 *Voyages dans les deux Siciles et dans quelques parties des Apennins. Traduits par G. Toscan.* Paris, 1800. 6 tom.

3 *Travels in the two Sicilies and some parts of the Apennines.* London, 1798. 4 vols.

4 *Rapports de l'air avec les êtres organisés.* Geneva, 1807. Trans. by J. Senebier.

The first important work by Spallanzani was his *Saggio di osservazioni microscopiche relative al sistema della generazione di Signore Needham e Buffon* (Modena, 1765). This work, like those that followed it, exhibits a clear and forceful style. It is quite free from the tedious prolixity that characterizes much of the scientific writing of the century, and it possesses the merit of being easily comprehended and analysed. The reader cannot fail to be impressed by its sane and modest criticisms, and by its rigorous logic.

In this work Spallanzani dealt with the generation of organized beings, and combated the views of Needham and Buffon on the nature of the animalculæ of infusions. Spallanzani showed that these were not mere wandering "organic molecules" as Buffon suggested, but distinct individual organisms, which like all animals and plants arose from seeds or germs. This was a preliminary to his work on spontaneous generation, the results of which were embodied in the *Opuscoli di fisica animale e vegetabile* (Modena, 1776). Spallanzani's researches on spontaneous generation were conducted with great precision, and his proofs, both positive and negative, were so varied and forceful, that his position was almost unassailable. In fact his skilfully conducted experiments permit us to compare him with Pasteur.

No less remarkable were Spallanzani's investigations on the regeneration of parts of lower animals. These researches were published in *Prodroma di un opera da imprimersi sopra le reproduzioni animali* (Modena, 1768). Spallanzani proved that snails, newts and worms can renew mutilated or missing parts. Shortly afterwards there appeared his work on the circulation, *Dei fenomeni della circolazione osservata nel giro universale de' vasi . . .* (Modena, 1773), in which he made microscopical observations on the circulation of the blood in cold-blooded animals and in the chick embryo. Very little notice has been taken of this treatise, although with his work on fertilization it certainly ranks as a classic in the history of embryology.

Spallanzani's researches on digestion, commenced about 1776, were published in his *Opuscoli di fisica animale e vegetabile* and in the *Dissertazioni di fisica animale e vegetabile* (Modena, 1780). These proved in a decisive manner that digestion is not a simple mechanical process, but one of true solution, occurring mainly in the stomach under the influence of the gastric juice.

The *Opuscoli* also contain some remarkable observations on moulds. Spallanzani investigated their morphology, the conditions necessary for their growth, their reproduction by spore formation, and the resistance of these spores towards heat and desiccation. He further observed that the spores of moulds only develop in certain media, and that they are disseminated throughout the air. Moulds spring up by these spores alighting on decomposing organic matter.

Spallanzani's earlier work on respiration, which appeared in his *Opuscoli* of 1776, consisted of an examination of the effect of a limited supply of air on living beings. Thus he found that certain animalculæ could live for long periods without much air, and that certain seeds could germinate in an enclosed volume of air. He further noted that cold-blooded animals can endure deprivation of air longer than warm-blooded ones. Death resulting from lack of air is due, according to Spallanzani, to the presence of a lethal vapour in expired air that acts upon the nervous system. These earlier researches, which appeared before Lavoisier's fundamental work on respiration (1777-1790), were considerably extended in Spallanzani's later years, and the results published in 1803, at Milan, in a posthumous work entitled *Memorie sulla respirazione.*[1] In this work Spallanzani described important observations on external influences affecting respiration, such as temperature and atmospheric pressure, and he arrived at the highly important conclusion that the tissues of the organism respire as well as the organism as a whole. He also made the fundamental discovery that animals placed in an atmosphere devoid of oxygen continue to give out carbon dioxide.

[1] Translated into French by J. Senebier, *Rapports de l'air avec les êtres organisés.* Geneva, 1807.

Spallanzani's investigations into the nature of fertilization were published in Italian in 1780.[1] He concluded that the ova of higher and lower organisms do not develop without the seminal fluid of the male, which fertilizes them. By the artificial fertilization of the eggs of the frog and tortoise, and by the successful introduction of seminal fluid into the uterus of a bitch, he showed that the development of the ovum is dependent upon the activity of the seminal fluid, but he erroneously concluded that it was the fluid medium and not the spermatozoa that caused fertilization. This error was corrected in 1824 by Prevost and Dumas, who showed that filtration destroyed the fertilizing power of the fluid. Spallanzani had previously (1771) made some observations on the microscopy of the semen of human beings and various animals, and the resistance of the spermatozoa to external influences.

Studies on Spontaneous Generation.

Of old the idea prevailed that certain organisms arose from putrescent matter, as vermin were thought to arise from filth. The doctrine of spontaneous generation occupied a place in the system of Aristotle[2] (384-322 B.C.), and indeed until the experiments of the later seventeenth century such a view of life could hardly be denied since it seemed self-evident. Van Helmont[3] (1577-1644), who possessed one of the keenest intellects of his day, may be cited as one who shared Aristotle's view, and Joachim Jung (1587-1657) was perhaps the first who threw doubt upon it.

The seventeenth century saw the extensive use of the magnifying glass and the invention of the microscope. These gave a new view of animate life. Giuseppe Aromatari[4] (1586-1660) insisted that all plants arise from seed and all animals from the egg. In 1651 William Harvey[5] (1578-1657) put forward the same view in his well-known dictum, *Ex ovo omnia*. Francesco Redi (1626-1697)[6] took the first step in the scientific refutation of spontaneous generation by proving experimentally that the flesh of dead animals does not engender worms unless the ova of live ones be first deposited on the flesh (1668). From this time onwards it was widely accepted that readily visible organisms were not propagated by spontaneous generation.

As regards minuter forms of life, the matter was complicated by microscopic progress. In 1683 A. von Leeuwenhoek (1632-1723) discovered the organisms that we now call bacteria, and it was soon found that swarms of these organisms appeared with infusoria in putrid organic matter. An hypothesis soon arose, which, whilst accepting the generation of the higher forms of life from seed, held that microscopic organisms were produced spontaneously from non-living matter. This view, held among others by Leeuwenhoek,[7] was not finally refuted until the advent of Pasteur. Whilst Redi had a considerable following, there were still many who opposed the doctrine of universal biogenesis.

Réaumur[8] (1683-1757) and Vallisneri[9] (1661-1730) warmly opposed belief in spontaneous generation. The latter writer was also one of the originators of the theory of pre-existing germs, a doctrine diametrically opposed to that of spontaneous generation, although it had then little experimental support to recommend it.

1 Translated into French by J. Senebier, *Expériences pour servir à l'histoire de la génération des animaux et des plantes*. Geneva, 1785.

2 Aristotle, *Historia animalium*. Lib. V, Cap. 1 ; Lib. VI, Cap. 15-16.

3 J. B. Van Helmont, *Ortus medicinæ*. Amsterdam, 1648. Pars. 1, tract XXI, p. 113, § 9.

4 G. Aromatari, *De rabia contagiosa*. Venice, 1625. And *Epistola de generatione plantarum ex seminibus*. Venice, 1625.

5 W. Harvey, *Exercitationes de generatione animalium*. London, 1651, p. 189.

6 F. Redi, *Experienzi intorno alla generazione degl' insetti*. Florence, 1668.

7 A. von Leeuwenhoek, *Arcana naturæ detecta*. Leyden, 1695. Epistola 75, pp. 307-320.

8 Reaumur, *Mémoires pour servir à l'histoire des insectes*. Paris, 1738. 6 vols. Vol. 1, p. 413, etc.

9 A. Vallisneri, *Opere fisico-mediche*. 3 tom. Venice, 1733. T. II. Pt. II, Cap. XX, p. 199.

In this connection reference should be made to Joblot[1] (d. 1725), an obscure French writer of the early seventeenth century, who experimentally combated the doctrine of a biogenesis as far as microscopic beings were concerned. He believed that the seeds of micro-organisms are disseminated throughout the air or are deposited on certain objects, and that they develop only on alighting in suitable media, from which they receive nourishment. The Englishman Henry Baker[2] (1698-1774) also pointed out in 1743 that the appearance of organisms in infusions is due to the seeds of the organisms developing, and not to any spontaneous growth from dead matter. Baker agreed with Joblot in ascribing the appearance of minute organisms in decomposing matter to their production from air-borne seeds.[3]

A retrograde step was taken by John Turberville Needham[4] (1713-81). He rejected the conception of the generation of micro-organisms from seeds in the air, in favour of Buffon's view that in all organisms there existed certain organic molecules, which on the death of the organism became re-organized into small microscopic beings. With the aid of these preconceived views, Needham performed his experiments about 1745. He boiled animal and vegetable infusions in flasks that were afterwards well corked and allowed to stand. Sixty to eighty tests were thus made, and organisms ultimately developed in all the infusions. The corking up of the flasks, explained Needham, ruled out the theory of seeds or germs entering them from the atmosphere. According to him the organisms were produced by a "vegetable force residing in every microscopical point of animal or vegetable matter."[5]

These views were popularized by the Comte de Buffon (1707-1788) in his *Histoire Naturelle*[6] (1749-67). There he put forward his doctrine of organic molecules. Buffon assumed that all animals and vegetables and all their parts contained a large number of living organic molecules, and that these formed the common unit of animals and plants. After death the organic molecules of the once living body became rearranged to form micro-organisms. Hence the micro-organisms of fermentation were formed by the reunion of organic molecules and not from seeds of their own kind. Generation and death were held to consist of processes of rearrangement of these organic molecules.

The views of both Buffon and Needham attracted widespread attention. They were strongly opposed by Spallanzani and by his close friend Charles Bonnet (1720-93). Bonnet expounded and defended the doctrine of pre-existing germs.[7] All beings according to him were already pre-formed in the germ, the development, unfolding (*evolutio*) and nutrition of which constituted generation.[8] He argued that the organisms in decomposing liquids ultimately came from air-borne organisms or their germs.

It was Spallanzani who proved that microscopic organisms were not spontaneously generated in the sense assumed by Needham and Buffon. His first important work, *Saggio di osservazioni microscopiche relative al sistema della generazione di signori Needham e Buffon* (Modena, 1765), was an attack on the systems of these naturalists. Spallanzani's position was further maintained in the

1 L. Joblot, *Descriptions et usages de plusieurs nouveaux microscopes* . . . . Paris, 1718. Ch. XVIII. See pp. 39-46, and p. 52.

2 H. Baker. *The microscope made easy.* London, 1743. Pt. II. Ch. 1.

3 *Ibid.*, pp. 69-70, 149.

4 J. Needham, *Summary of some later observations upon generation, corruption, and decomposition of animal and vegetable substances.* London, 1749.

5 *Ibid.*, pp. 36, 39, 30-32, 46-48.

6 G. L. Le Clerc, Comte de Buffon, *Histoire naturelle, générale et particulière.* Paris, 1749-1769. 15 tom. T. 11, pp. 24, 302-5, 320, 424-26.

7 C. Bonnet, *Considérations sur les corps organisés.* Amsterdam, 1762. *Œuvres.* Neuchâtel, 1779-83. T. III, Ch. I and II.

8 *Ibid.*, p. 74. And *La palingénésie philosophique.* Geneva, 1769. T. I, p. 93.

treatise, *Opuscoli di fisica animale e vegetabile* (Modena, 1776),[1]. Most of the experiments on which he based his arguments were conducted between 1765 and 1770. It will be remembered that according to Needham a "vegetative force" resided in inert matter, causing under suitable conditions its metamorphosis into living matter. This force was supposed to be specifically determined for each class of animal, so that a certain kind of inert matter would always develop into a specific being. Moreover the force, the activity of which Needham ascribed to the Deity, was supposed to cause the transformation of inert plant matter into vitalized animal matter and *vice versa*.

Spallanzani maintained that Needham's "vegetative force" was a creation of the imagination. He showed that the mere corking of flasks containing alterable organic matter, as practised by Needham, rendered the experiment invalid, since the corks being porous admitted something from the air.[2] He introduced a new technique into his studies on spontaneous generation by employing hermetically sealed flasks. By boiling infusions for a long time in a flask and then hermetically sealing it, he proved that no organisms were generated as long as the flask remained sealed. In fact such infusions kept indefinitely unless the seal was broken.[3]

It is to Spallanzani that we owe the explanation of sterilization by heat, and the discovery that previously sterilized organic matter can be preserved in hermetically sealed vessels. This discovery was pressed into service by Scheele (1742-1786), who in 1782 utilized it for the preservation of vinegar, and by Appert, a Parisian cook, who preserved foods by exposing them in hermetically sealed vessels to the temperature of boiling water.

Yet Needham clung to his doctrine of "vegetative force," with its implication of spontaneous generation. He maintained that organisms did not develop in the sealed flasks in Spallanzani's experiments because the strong heating destroyed the "vegetative force," and because this force was rendered inoperative "by the diminished elasticity of the air."[4] These objections were rigorously examined by Spallanzani.[5] If the so-called "vegetative force" were annihilated or enfeebled by heat, then, argued Spallanzani, a prolonged and vigorous heating of an infusion should destroy this force, and consequently no organisms would appear. In other words the number of organisms should be inversely proportional to the degree and duration of the heating.[6] To test this Spallanzani took nineteen infusions, boiled some for a short time, others longer, and the rest for a longer period still. The flasks were then loosely corked, left for some time, and then examined for micro-organisms. The results clearly showed that long boiling of seed infusions did not prevent the formation of organisms, but that infusions longest boiled contained most organisms.[7] In fact the number of organisms was directly proportional to the duration of boiling, not inversely proportional as Needham insisted. Spallanzani suggested that heat has a decomposing or disintegrative effect upon the animal or vegetable matter of infusions, and consequently the more the latter is resolved the more easily it is assimilated by micro-organisms. Thus it is that these appear and develop quicker in a boiled infusion of seeds than in an unboiled infusion.[8]

Spallanzani made further attempts to see if the degree of heating of infusions influenced the number of micro-organisms that could subsequently develop in them.

1 Spallanzani's work relative to spontaneous generation is in *Opus* I.

2 *Ibid.*, Pt. I, Cap. I, p. 12.

3 *Ibid.*, p. 12.

4 Needham, quoted by Spallanzani, *op. cit.*, Cap. II, p. 14.

5 Spallanzani, *ibid.*, Cap. II.

6 *Ibid.*, Cap. II, p. 14.

7 *Ibid.*, pp. 15-22.

8 *Ibid.*, Cap. II, pp. 20-21.

According to Needham strong heat should entirely destroy the "vegetative force" of an infusion. Eleven kinds of seeds were roasted, carbonized, heated by hot coals and blowpipes, and then infusions made with the residues and distilled water. Spallanzani still witnessed, however, the production of micro-organisms in these infusions.[1] "These facts only convince me," he concluded, "that plant seeds never fail to produce micro-organisms when exposed to any degree of heat. Hence 'vegetative force' is nothing but the work of imagination. If no organisms appear in vessels hermetically sealed and kept an hour in boiling water, their absence must proceed from some other cause."[2]

Needham had argued that the sealing of flasks had diminished the elasticity of the contained air and so prevented the growth of organisms.[3] Spallanzani tested the validity of this assertion by preparing infusions as before, but he drew out the necks of the flasks to capillary fineness. This capillary neck could be quickly sealed in the blowpipe without heating the air contained in the flask. No organisms developed in infusions well-boiled before sealing the flasks.[4] As a further test he sealed up infusions in vessels containing both rarefied air (*i.e.*, air of "diminished elasticity") and compressed air, and immersed the vessels in boiling water for periods varying from half a minute to two minutes. But organisms appeared in every case when the vessels were cooled and left for some days.[5]

From these experiments Spallanzani drew two conclusions.[6] (*a*) Heat deprives sealed-up infusions of the micro-organisms they contain. This is evident since micro-organisms appear in unboiled infusions in open and closed vessels, but do not appear in well-boiled infusions in hermetically sealed flasks. The mere closing of the flasks cannot be the cause of their absence. (*b*) The heating of infusions to boiling point for one hour kills mature micro-organisms.[7]

This work of Spallanzani on sterilization is most startling in its modernity. It shows that Pasteur had an able predecessor. Having effectively refuted Needham's views on spontaneous generation, Spallanzani was compelled to explain why micro-organisms appear in infusions of dead organic matter. "If micro-organisms do not originate by the agency of 'vegetative force' we must ascribe their origin to eggs, seeds, or pre-organized corpuscles, which I distinguish by the generic name of germs."[8] According to Spallanzani these germs are so small in size that they penetrate the smallest pores and openings, and this explains the results obtained by Needham in favour of spontaneous generation, since he used corked vessels. "We are led to ascribe the origin of micro-organisms," wrote Spallanzani, "to germs in the medium in which they develop. For a limited time the germs resist the influence of heat, but at length they succumb to it. The micro-organisms appearing in infusions in open flasks exposed to the temperature of boiling water, or to the flame of the blowpipe, do not appear because their germs have resisted so great a degree of heat, but because other germs have entered the infusions from without after the heat has been withdrawn."[9]

A further controversy resulted between Spallanzani and Needham on the origin of micro-organisms. Needham, whilst accepting the animal nature of animalculæ, believed that they were derived by a kind of metamorphosis from plant matter under the influence of "vegetative force." According to Needham's account, "plant matter

1 *Ibid.*, Cap. II, pp. 22-24.
2 *Ibid.*, p. 24.
3 Quoted by Spallanzani, *op. cit.*, Cap. III, p. 25
4 *Ibid.*, Cap. III, pp. 26-27.
5 *Ibid.*, pp. 28-29.
6 *Ibid.*, p. 38.
7 *Ibid.*, p. 39.
Ibid., p. 40.
9 *Ibid.*, pp. 42-43.

swells up and is filled with a limpid liquid, which finally produces globules. These globules are truly animated, and run hither and thither with all the characteristics of ordinary microscopic beings."[1] Curiously enough similar views were held by two nineteenth-century microscopists, Frémy[2] and Trécul.[3] Spallanzani's careful microscopical examination of seeds and plant matter in a state of decomposition failed to verify any stage in this supposed metamorphosis of inert plant matter into living animal matter. He firmly denied the transformation, and by his skilfully conducted observations reduced Needham's system of generation to a gross absurdity.[4]

Discussing the problem of the origin of the micro-organisms in infusions, Spallanzani considered that these must either have pre-existed in the organic matter in which they later appeared, or else that they must have come from exterior germs.[5] If the organisms pre-existed in the organic matter they should still preserve their vitality in the absence of the fluid of an infusion. Actually he found that they perished on the evaporation of the liquid in which they first made their appearance.[6] But their germs resisted desiccation to a considerable degree. Hence Spallanzani accepted the view that germs or little eggs passed from the air into infusions and gave rise to micro-organisms. Provided that he destroyed the organisms of infusions by heat and kept them from the air, he observed that no fresh organisms were produced, but that they soon developed in the presence of air. Accepting the view that the new organisms had their origin in germs, he was convinced that the germs must have come from the air.[7] In answer to the objection that such germs could not be seen, Spallanzani replied, "It matters little whether these germs or seminal principles are visible or no. Invisibility is no proof of non-existence. The germs may be either too transparent or too minute for perception."[8]

As final proof that the germs of micro-organisms must ultimately come from the air, Spallanzani performed the following experiments.[9] Sixteen large vessels containing infusions were divided into groups of four. One group was hermetically sealed; one closed with well-fitting wooden stoppers; one closed with cotton; and one left open. The contents of all sixteen flasks were boiled for an hour, left for a month, and then examined. The vessels that had free communication with the air were full of micro-organisms, those stopped with cotton contained about a third of the number found in the open vessels, and slightly exceeded the number of organisms in the flasks with wooden stoppers. The hermetically sealed vessels contained the fewest organisms of all. From these observations Spallanzani concluded that the rate at which micro-organisms develop in infusions is proportional to the degree of communication with the external air. "Micro-organisms are derived from germs brought by the external air, or from germs mixed with the infusions. Air is their vehicle and it should convey a larger number of germs into open vessels than into those partially closed or into which the air can only penetrate with difficulty, as in vessels plugged with cotton or wood. The volume of air included in hermetically sealed vessels will produce the organisms that appear, but these will be few compared to those in the open or partially closed vessels."[10]

1 Needham, quoted by Spallanzani, Pt. II. Cap. VIII, pp. 125-6.

2 E. Frémy, *Sur la génération des ferments*. Paris, 1875.

3 A. Trécul, 'Remarques sur les levures alcoöliques et lactiques.' *Comptes rendus de l'Académie*. lxxv, pp. 1066, 1160, 1169. 1872.

4 Spallanzani, *op. cit.*, pp. 127-136.

5 *Ibid.*, Parte II. Cap. XI, p. 196.

6 *Ibid.*, p. 197.

7 *Ibid.*

8 *Ibid.*, p. 200.

9 *Ibid.*, Cap. XI, pp. 200-201.

10 *Ibid.*, pp. 201-202.

Spallanzani had observed that the germs of micro-organisms can resist adverse conditions more easily than the micro-organisms themselves. Thus whilst the mature micro-organisms succumbed to low temperatures, boiling water, and desiccation, their germs were unharmed after exposures lasting the same time.[1] This explained why the short boiling of an infusion never rendered the liquid sterile. The heat destroyed the mature organisms but not their germs. Incidentally by discovering that moist heat exerted a more destructive effect upon germs than dry heat, Spallanzani introduced a very important principle of sterilization.[2] He knew that moulds withstand a dry heat much above 100° C. for some time, but succumb when left in steam or boiling water for a like period.[3]

In his masterly researches on the origin of moulds, Spallanzani demonstrated that these organisms are not spontaneously generated. He described with great accuracy the external morphology of various moulds, their organs of fructification, and their conditions of growth.[4] He obtained mould spores in the form of a fine dust from the sporangia and sowed these spores in suitable media.[5] New moulds soon developed, but not when the spores were sown in media devoid of nutritive material, e.g. stones, glass, paper.[6] That these seeds were the true seeds of moulds was further established by showing that they always gave rise to the same species of mould from which they were derived.[7] Finally he further refuted the view that moulds were generated spontaneously by enclosing bodies subject to mouldiness in flasks, some of which were open to the air while others were provided with a fine capillary tube.[8] Moulds appeared in all cases, but those exposed most to the external air had a more prolific growth than others. He then hermetically sealed small vessels containing organic media suitable for the development of moulds, and plunged the vessels for several hours in boiling water. No mould developed after a considerable period, nor did it when the organic matter was sterilized and then kept *in vacuo*.[9] Spallanzani thus proved that the ultimate origin of mould spores is the air.

These brilliantly conducted and interpreted experiments of Spallanzani on spontaneous generation, and his remarkably modern explanations, can only be appreciated by a perusal of Pasteur's work on the subject. Unfortunately Spallanzani's work in this direction bore no immediate fruit. In the next century it supplied a link in the biogenetic theory of fermentation by stimulating the interest of a small group of writers, among whom we may mention Gay-Lussac (1778-1859), Schultze (1815-73), and Schwann (1810-82). The researches of these investigators on spontaneous generation also threw much light on the nature of fermentation. By improving the methods invented by Spallanzani they attempted to prove that air-borne micro-organisms and their germs are the real cause of fermentation and putrefaction. These investigators were the originators of the biogenetic theory of fermentation.

Spallanzani on Digestion.

The seventeenth century physiologists generally held digestion to be a particular kind of fermentation. Van Helmont [10](1577-1644) believed that gastric digestion

1 *Ibid.*, Parte I. Cap. IV, pp. 52, 60, 65-68. Parte II. Cap. XI, p. 197.

2 *Ibid.*, Cap. IV, pp. 56-57.

3 *Osservazioni e sperienze intorno all'origine delle piantine delle muffe.* Vol. II, pp. 257-277, in the *Opuscoli di fisica animale e vegetabile.* Modena, 1776. See pp.270-272.

4 *Ibid.*, pp. 258-261.

5 *Ibid.*, p. 266, etc.

6 *Ibid.*, p. 270.

7 *Ibid.*, p. 268.

8 *Ibid.*, pp. 274-5

9 *Ibid.*, p. 275.

10 Van Helmont, *Ortus medicinæ.* Amsterdam, 1648. Tract XXI, p. 209, § 2; p. 210, §§ 12-13.

depended upon an acid ferment.[1] Sylvius (1614-72) and his pupils regarded digestion as a dissolution of food into assimilable matter by fermentation, in which the saliva and pancreatic juice played the principal rôle.[2] Regnier de Graaf[3] (1641-73), who discovered pancreatic juice in 1664, maintained that this fluid was one of the fundamental secretions in digestion. Further anatomical and physiological researches by Peyer[4] (1653-1712) and Brunner[5] (1653-1727) served to support the belief in the occurrence of ferments in the alimentary tract. On the other hand, Borelli[6] (1608-79) and the iatro-physical school held that digestion resulted from the trituration of food within the stomach. In his inaugural dissertation, *De intestinis*[7] (1684), Stahl (1660-1734) implied that saliva and pancreatic juice played an important part in digestion, which he regarded as a special type of fermentation controlled by "the energy of the soul."[8] Boerhaave[9] (1668-1738) effected a synthesis of the iatro-chemical and physical views by regarding digestion as a kind of solution aided by trituration. He admitted that the stomach contents under the action of heat underwent "an attenuated fermentation," different from that occurring outside the body. Albrecht von Haller (1708-77) accepted the view that the gastric juice exerted a softening effect on food, eventually macerating or dissolving it. Yet he did not consider that the change was effected by a ferment, but rather by a kind of incomplete putrefaction.[10]

These various views on digestion were tested by Réaumur[11] (1685—1757), who in 1752 proved digestion to be mainly the result of the solvent action of the gastric fluid. He caused a kite to swallow food contained in hollow metal tubes open at both ends. The tubes being rejected *per os* were examined, and Réaumur found that the food they contained was softened and bitter to the taste.[12] He obtained gastric juice by administering to the bird hollow perforated tubes containing sponges. After recovery of the tubes the sponges yielded some fifty to sixty minims of an opaque, cloudy, yellowish-white and salt-tasting acid juice.[13] With this Réaumur attempted to perform digestion *in vitro*, but he found that the fluid, although softening food, did not completely digest it.[14] We note that he made no attempt at keeping the food at body temperature.

Some twenty-four years elapsed before the French writer's researches were continued and extended by Spallanzani. His discoveries on digestion, although conducted during the years 1776-7, were not published in collected form until 1780.[15]

1 *Ibid.* Tract XXI, pp. 208-225. See also author's article, "Van Helmont on Fermentation," *Archiv f. Geschichte der Math. Naturwiss. u. d. Technik.* Bd. 12. Heft 1, p. 70. Leipzig, 1929.

2 Sylvius, *Opera medica.* Amsterdam, 1679. *Method. med.* Lib. 1. Cap. I, § 18; Cap. XVI, § 6. *Praxis. med.* Lib. 1. Cap. VII, p. 166.

3 Regnier de Graaf, *Tractatus anatomico-medicus de succi pancreatici natura et usu.* Leyden, 1671. pp. 65-6, and elsewhere.

4 J. C. Peyer, *De glandulis intestinorum exercitatio.* I. Cap. II. See his *Parerga anatomica et medica.* Geneva, 1681.

5 J. C. Brunner, *Experimenta nova circa pancreas.* Amsterdam, 1682. *Dissertatio inauguralis de glandulis duodeni*, 1687.

6 A. G. Borelli, *De motu animalium.* Rome, 1680-81. I, p. 287.

7 G. E. Stahl, *Dissertatio medica inauguralis de intestinis.* Jena, 1684. See also Stahl's *Theoria medica vera.* Hala, 1708. De nutritioni, p. 470.

8 *Ibid.*, p. 472.

9 H Boerhaave, *Institutiones medicæ.* Leyden, 1708, pp. 21-23.

10 A. von Haller, *Elementa physiologiæ corporis humani.* Lausanne, 1757-65. 8 tom. T. VI, pp. 297, 330, 331; T. VII, pp. 71, 51.

11 R. A. F. de Réaumur, 'Sur la digestion des oiseaux.' *Mémoires de l'Acad. des Sciences.* Paris, 1752, pp. 266-307, 461-495.

12 *Ibid.*, pp. 469-70.

13 *Ibid.*, pp. 483-4.

14 *Ibid.*, pp. 485-6.

15 Spallanzani, *Dissertazioni di fisica animale e vegetabile.* Modena, 1780. 2 vols. Vol. I contains his work on digestion.

Réaumur had experimented with only a few animals, but Spallanzani went further and experimented with a large number, himself among them. His first dissertation was concerned with the digestion of birds with strong stomach muscles. Since Borelli (1681) it had been argued that these birds digested their food by the mechanical trituration of the gizzard, and this conclusion was falsely extended to explain digestion generally by the iatro-physical school. Spallanzani improved on Réaumur's perforated tubes by substituting cylindrical metal vessels open at each end, the two apertures being covered by wire gauze.[1] He confirmed Réaumur's observation that various hard seeds whilst kept within the metal tubes remained undigested in the stomachs of the birds, although unprotected seeds given as a control were speedily digested.[2] In other tests he used pierced hollow spheres of metal and wood to hold the food, so that the gastric juice would penetrate more easily.[3] The spheres were recovered by the mouth or by opening the animal. Spallanzani was forced to draw the same conclusion as Réaumur, namely that the chief factor in the digestion of certain birds is the trituration or mechanical muscular action of the coats of the stomach.[4] This appeared obvious from the fact that glass was pulverized and thin hollow tubes were crushed on passing through the gizzards of such birds.[5]

It had been suggested by Redi and Réaumur that the small stones found in the gizzards of certain birds were necessary for digestion, acting presumably by triturating the food.[6] Spallanzani controverted this view, since he observed that birds deprived of such stones still digested their food.[7] He further showed that trituration resulted from the peristalsis of the gastric muscles, and that by breaking up the food trituration aided digestion.[8] He demonstrated this by administering to birds chopped food in hollow tubes. On recovering the tubes much of the food was found to be digested.[9]

At this point Spallanzani made experiments on artificial digestion, or digestion *in vitro*. He extracted a considerable quantity of gastric juice from the stomachs of various birds, describing the yellow fluid he obtained as a limpid liquid with a bitter and salt taste.[10] Spallanzani then placed macerated food in the gastric juice, and kept the whole at body temperature for three days. It will be noted that Réaumur failed to observe this precaution and thus obtained unsatisfactory results. In each of Spallanzani's tests digestion, although not complete, was well advanced, and by repeated additions of gastric fluid the food eventually became entirely dissolved. In a control experiment he placed food in water instead of gastric juice. Signs of slight putrefaction soon set in, but the food remained undigested.[11]

The chief subject of Spallanzani's second group of researches was a crow. This animal proved exceedingly useful because it vomited every two or three hours anything it could not digest.[12] It was forced to swallow hollow silver tubes and spheres containing various foods, and after three hours the metal objects, being of an indigestible nature, were vomited. An examination of their contents was then made.[13] By repeatedly administering the same food in the same tube Spallanzani

1 *Ibid.* Diss. I. § III.
2 *Ibid.* § IV.
3 *Ibid.* § VII.
4 *Ibid.* § VIII.
5 *Ibid.* §§ X-XII, XV-XIX.
6 *Ibid.* § XXIII.
7 *Ibid.*, §§ XXVIII and XXX.
8 *Ibid.*, §§ XXIX and XXXIV.
9 *Ibid.*, §§ XXXIX and XLIII.
10 *Ibid.*, § LVI.
11 *Ibid.*
12 *Ibid.* Diss. II. § LIX.
13 *Ibid.* § LXI.

was able to subject the food to the action of the gastric juice for any period of time he pleased. These experiments proved that visible signs of gastric digestion appeared in about an hour, and that in about seven hours most food was rendered completely fluid. Vegetables, fruit and bread were digested more easily than meat.[1]

Spallanzani further proved that the rate of digestion is proportional to the amount of gastric juice surrounding the food.[2] Thus food enclosed in tubes was digested far more slowly than that constantly surrounded by the gastric fluid. This was ascertained by causing the bird under observation to swallow food tied to string or wire, so that it could be pulled up after a given time and its state compared to that of food administered in metal tubes.[3] Spallanzani attributed the more rapid solution to the free action of the gastric juice.

By tying sponges to the end of a wire and making the crow swallow the sponges, which he afterwards withdrew, Spallanzani obtained further supplies of gastric juice. This fluid was also obtained by making the crow swallow metal tubes containing sponges, which were recovered full of gastric juice after the bird had vomited the tube. He observed that the fluid had similar characteristics to that obtained from other birds.[4] It was bitter and salt to taste, and when cold had no more action on food than ordinary water, although when kept at the body temperature it speedily produced the dissolution of food. Similar artificial digestions were brought about with the gastric juices of a large number of animals. Obviously the gastric juice obtained was not pure. It was a mixture of saliva, juice secreted by the œsophagus, possibly pancreatic juice, and bile, which accounted for its bitter taste.

Yet Spallanzani did not fail to notice that digestion *in vitro* occurred more slowly than in the stomach.[5] He ultimately concluded that this was due to the constant renewal of gastric juice in the stomach. The body undergoing digestion was constantly bathed in the fluid, whilst the substance undergoing change *in vitro* was surrounded by a very limited quantity of juice that was never renewed.[6] Spallanzani confirmed this view by allowing gastric juice to drop very slowly on to pieces of meat, which were rapidly digested. The same quantity of juice proved less efficacious when acting on meat in small tubes.

The general conclusions that Spallanzani drew from these experiments on various birds were confirmed by further researches on other animals.[7] These all showed that gastric fluid causes digestion by its dissolving action on food. During his experiments on birds Spallanzani paid special attention to the comparative digestibility of different animal tissues. He observed that fleshy and soft parts were easily digested, but bones, horn, hard skin and hair were usually unaffected, although tests on some birds showed that they could slowly digest bone.[8] Spallanzani further noted that the gastric juice is specific for each type of animal. Thus he discovered that the gastric fluid of ruminants is specially adapted to the digestion of grass and fodder, whilst carnivorous animals secrete a fluid particularly potent for flesh but not for vegetable foods.[9] Special interest is attached to his observation that under the stress of starvation animals will gradually accustom themselves to a new diet. He induced carnivorous animals to become herbivorous, and *vice versa*.[10] The administration of tubes containing food to ruminants did not result in successful digestion because the food could not then be

1 *Ibid.* §§ LXII-LXV.
2 *Ibid.* §§ LXVI-LXVIII.
3 *Ibid.* § LXVIII.
4 *Ibid.* §§ LXXXI-LXXXIII.
5 *Ibid.* § LXXXVIII.
6 *Ibid.* § XCI.
7 *Ibid.* Diss. III.
8 *Ibid.* §§ XCVII-XCVIII; Diss. II. §§ CXLVIII, CLVII, CLXXXIII; Diss. V. § CXCVI.
9 *Ibid.* Diss. IV. § CLXIX.
10 *Ibid.* CLXXV.

ruminated. To overcome this difficulty Spallanzani thoroughly masticated the food before placing it in the tubes. These were then given to the animal, and an examination of the tubes after they had been voided showed that digestion was complete. Spallanzani thus established the fact that ruminants only digest macerated food, the maceration being accomplished by the constant rumination. This process is analogous to trituration in the case of certain birds.[1]

Spallanzani regarded digestion as a process occurring mainly in the stomach. He was however aware of the softening action of the saliva, and his investigation of the juice secreted by the œsophagi of certain birds proved that this undoubtedly starts the digestion that continues in the stomach. In the dissertation where he deals with human digestion he expresses the opinion that although digestion occurs mainly in the stomach it is perfected in the intestines.[2] Spallanzani believed that the gastric juice had its origin in the glands of the stomach, since they appeared to secrete a fluid that continually reappeared when wiped off. He did not collect enough fluid from the glands of an isolated stomach to test this view thoroughly.

It is noteworthy that Spallanzani was the first to conduct extensive observations on human digestion within the living body. Rather than rely on analogy he experimented on himself. During his observations on an eagle he caused the bird to swallow meat tied up in a small linen bag, which was examined after being voided. No meat was found in it, and this suggested that the meat had been rendered soluble and had diffused through the linen bag into the stomach or intestines.[3] Spallanzani was prompted to experiment on himself in the same manner and he courageously swallowed food contained in metal tubes, wooden spheres, and linen bags. He found that the food contained in linen bags was perfectly digested when these were voided, although imperfect digestion resulted when the food was not thoroughly masticated.[4] Mastication, Spallanzani pointed out, is an important aid to human digestion, and takes the place of trituration in some birds.[5] Trituration plays no part in human digestion because food is still digested when enclosed in small wooden spheres.[6] Soft and hard bones included other articles of this worthy physiologist's diet. The soft bones were digested but not the hard.[7]

Wishing to obtain some of his own gastric juice Spallanzani first considered swallowing tubes containing sponges, hoping that they would be vomited later. He finally decided to take the safer course of making himself vomit on an empty stomach, but after one or two trials declared that his curiosity could not conquer his repugnance.[8] He described the juice he obtained as a thick, foaming, saline liquid, and he successfully carried out digestion *in vitro* by means of it. As in previous cases, it was necessary to maintain both food and gastric juice at body temperature.[9]

According to Boerhaave[10] food underwent a putrefaction or fermentation in the stomach, where warmth, moisture, and the residue of previously digested food promoted the process. He further considered that trituration played an important rôle in the digestion of hard food. Spallanzani experimentally controverted these views. He showed that, except in the case of certain birds, trituration is a negligible factor in digestion, and he disproved Boerhaave's view that the residue of already

1 *Ibid.* Diss. III. §§ CXXXIX-CXL, CXLIV.
2 *Ibid.* Diss. V. § CCXIV.
3 *Ibid.* Diss. IV. §§ CLXXX-CLXXXI.
4 *Ibid.* § CCIV.
5 *Ibid.* § CCXI.
6 *Ibid.* § CCVIII.
7 *Ibid.* § CCXIV.
8 *Ibid.* § CCXV.
9 *Ibid.* §§ CCXVI-CCXVII.
10 H. Boerhaave, *Institutiones medicæ.* Leyden, 1708, pp. 21-23.

digested food aids digestion. In fact he observed that digestion is more rapid and efficacious on an empty stomach.[1]

In 1772 John Hunter (1728-93), the celebrated English surgeon and anatomist, directed his attention to the problem of digestion.[2] He examined the stomachs of animals and humans after death, and recorded that the wall of the stomach was partly digested. This he ascribed to the continuance of normal digestion after death, the gastric fluid dissolving the stomach itself when this was deprived of the vital principle.[3] Hunter considered that digestion took place independently of the warmth of the body. These observations were the beginnings of an animated controversy between Hunter and Spallanzani. Spallanzani failed to confirm the Englishman's observations, and only noted a few cases of softening of the stomach wall after death. Moreover his experiments showed that digestion does not occur at temperatures below that of the body.[4] Hunter[5] retorted by suggesting that Spallanzani was deficient in anatomical knowledge. This impolite criticism was answered in a dignified letter from Spallanzani in 1788.[6]

Observations on digestion after death were continued by Spallanzani. He noted that digestion continued for some hours after death, although at a much slower rate than during life.[7] Hunter was essentially a vitalist, and held the opinion that the action of the gastric juice depended upon some vital principle only met with in the body. It was shown however by Spallanzani that digestion resulted from the action of the gastric juice acting independently of any vitality or vital force, since he witnessed digestion in the stomachs of many animals several hours after death. In other experiments he isolated stomachs containing previously ingested food, which began to soften in about five hours and a half, although there was no connection with the living body.[8]

In his sixth dissertation Spallanzani discusses the nature of digestion. It was universally accepted in the latter part of the XVIIth century that digestion and in fact all physiological processes were types of fermentation. To quote Bellini[9] (1643-1704), a contemporary writer, "*Fermentorum et fermentationum plena sunt omnia.*" Spallanzani would not grant that a proper fermentation occurred during digestion because he had never observed effervescence taking place,[10] and moreover the contents of the stomachs of animals opened on a full stomach showed no signs of active fermentation.[11] Like most chemists of the century, Spallanzani still identified fermentation with a frothing or bubbling movement, with an "intestinal motion." As Spallanzani observed no such motion in food undergoing digestion, he concluded that no "sensible fermentation" occurred.[12]

During the eighteenth century a certain school of physiologists held the view that digestion was connected with fermentation of an acid nature. Spallanzani considered the evidence for and against this. He established the fact that partly digested food has an acid reaction, but ascribed this to the nature of the food.[13] It

1 Spallanzani, *op. cit.* §§ CCXX-CCXXI.

2 J. Hunter, 'On the digestion of the stomach after death.' *Phil. Trans. of Royal Society.* London, 1772. Vol. LXII, p. 447.

3 *Ibid.*, p. 449.

4 Spallanzani, *op. cit.* § CCXIV.

5 J. Hunter, *Lectures on the principles of surgery*, 1786-7. See his *Works*, London, 1835. 4 Vols. Vol. IV, pp. 81-121.

6 Spallanzani, *Lettera apologetica in riposta alle osservazioni sulla digestioni del Sig. Gio. Hunter.* See *Opuscoli scelti sulle scienzi e sulle arti.* Milan, 1788. T.XI, p. 45.

7 Spallanzani, Diss. IV. § CCXXV.

8 *Ibid.* §§ CCXXVI-CCXXVIII and CCXXXI.

9 L. Bellini, *Opuscula aliquot ad A. Pitcarnium.* Leyden, 1696. Cap., De fermentis et glandulis rursus, p. 178.

10 Spallanzani, *op. cit.* § CCXXXVII.

11 *Ibid.* § CCXXXVIII.

12 *Ibid.* § CCLXIV.

13 *Ibid.* § CCXLI

must not be forgotten that the chemical tests for acids and alkalis were far from perfect at this period. But Spallanzani's tests must have been hopelessly inadequate when he inferred that a vegetable diet rendered the chyle more acid than a meat diet, whereas the converse is the case.[1] According to him, the gastric juice that he examined had an acid taste, although he failed to confirm this chemically. From chemical tests both Spallanzani and his colleague Scopoli (1723-1788) concluded that gastric juice was a neutral saline body.[2] Spallanzani ascribed the acid taste and smell of the stomach contents to the tendency of food to sour, and hence he regarded these properties as abnormal. Although granting that food undergoing digestion was often acid, Spallanzani considered that the acidity disappeared before digestion was complete.[3]

Finding that he could not detect any acid in the gastric juice by ordinary chemical means, Spallanzani had recourse to a bio-chemical method. He knew that traces of acids coagulate milk, and that milk coagulates rapidly in the stomach. Accordingly he observed that an aqueous extract of the stomach membrane coagulates milk. Gastric juice itself has this property, and Spallanzani concluded that the coagulation was due to an acid which was latent since it did not respond to ordinary chemical tests.[4] It seems incredible that Spallanzani missed the acid nature of the gastric juice, the knowledge of which was fully grasped by van Helmont nearly a century and a half previously.[5]

Those physiologists who followed the doctrines of Haller held that digestion was a type of incomplete putrefaction. Spallanzani showed that digestion was totally opposed to putrefaction. In fact, he observed in controls kept at body temperature that digestion was over before putrefaction had time to commence. Whereas food was resolved into chyle in a few hours by gastric juice, putrefaction in controls kept in water did not set in until the corresponding number of days.[6] An examination of the stomach contents several hours after a meal revealed no sign of putrefaction.[7] Furthermore, Spallanzani observed that gastric juice even destroyed the putridity of slightly putrid meat, and for this reason he classed it as an "antiseptic."[8]

It is to Spallanzani and Réaumur that we owe the experimental recognition of the solvent power of gastric fluid. Spallanzani made a definite advance by proving that digestion did not correspond to putrefaction or to any type of fermentation known in his day. Although he recognized that digestion was not a fermentation in the then accepted sense of the word, he was at a loss to explain how the gastric juice acted upon the food. If he had insisted upon the acid nature of the gastric juice, Spallanzani would have probably short-circuited the history of the physiology of digestion by some fifty years. There is, however, a possible explanation of his failure to emphasize the acid reaction of the juice. Many of his tests on acidity were made on juice extracted from a fasting animal, and consequently such juice would not be so acid as that actively engaged in bringing about digestion. When he did detect acidity he considered it abnormal. Hunter originally regarded the acidity of gastric juice as being of some importance in digestion,[9] although later he attributed its presence to the decomposition of sugar in the food.[10] An important

1 *Ibid.* § CCXLIII.

2 *Ibid.* § CCXLIV.

3 *Ibid.* § CCXL.

4 *Ibid.* §§ CCXLV-CCXLVIII.

5 J. B. van Helmont, *Ortus medicinæ*. Amsterdam, 1648. Tract XXI, pp. 209, 210, 213, 214.

6 Spallanzani, *op. cit.* § CCL.

7 *Ibid.* §§ CCLI-CCLIII.

8 *Ibid.* §§ CCLV-CCLIV. The slight antiseptic action of gastric fluid is of course due to the hydrochloric acid it contains.

9 J. Hunter, 'On the digestion of the stomach after death.' *Phil. Trans.* 1772. LXII, p. 454.

10 J. Hunter, *Observations on certain parts of the animal economy*. London, 1786, p. 163.

step was made in 1785 by Carminati,[1] who showed that the gastric juice of carnivorous animals is scarcely acid in a starving animal, but strongly acid after feeding. These observations would have cleared up Spallanzani's difficulties, but it seems that he was unaquainted with them.

It was not until 1824 that Prout[2] suggested the presence of hydrochloric acid in the gastric juice. Tiedemann and Gmelin[3] proved its presence in this liquid in 1826. But the digestive ferments postulated by van Helmont were entirely forgotten, and it became the tendency to regard the active body in the gastric juice as an acid. In 1834, however, Eberle[4] re-advanced the conception of one or more gastric ferments causing digestion. It was through his researches and those of Schwann[5] (1810-1882) in 1836, and of Wasmann[6] in 1829, that our knowledge of the gastric ferments developed, and with it the recognition that digestion is a resolution of food by the agency of non-living ferments or enzymes secreted by the living tissues.

1 Carminati, *Ueber die Natur des Magensaftens.* Vienna, 1785.

2 Prout, *Journal de phys. exp.* IV, p. 294. Paris, 1824.

3 Tiedmann and Gmelin, *Die Verdauung nach Versuchen.* Heidelberg, 1826.

4 Eberle, *Physiologie der Verdauung auf natürlichen und künstlichem Wege.* Wurzburg, 1834.

5 T. Schwann, 'Über das Wesen der Verdauungsprozess.' *Müller's Archiv f. Anatomie, usw.* Heft. I, pp. 90-138. Berlin, 1836.

6 Wasmann, *De digestioni animali.* Berlin, 1839.

Section of Laryngology.

[*December* 6, 1929.]

Specimen: Larynx of a Patient who was Operated on by Laryngo-fissure for Epithelioma, showing no recurrence at his death twenty years afterwards.—Sir STCLAIR THOMSON, M.D.—The patient was a schoolmaster, aged 59, seen in January, 1909, with irregular, grey growth over middle of left cord. A portion was removed for biopsy, and the growth was reported to be a squamous-celled carcinoma (Cuthbert Lockyer, S. G. Shattock, H. T. Butlin). Operation on February 17, 1909. Patient continued his work as a schoolmaster for some years, and once when written to in reference to his habits, he replied: "I never have any trouble with my throat; I smoke no end and never stop talking"! He died from heart failure last winter (1928), with no recurrence of cancer anywhere, at the age of 79, and twenty years after the operation.

Mr. Colledge grades the malignancy in Group I.

Four Cases Illustrating some Points in Subglottic Cancer of the Larynx, and the Condition Four, Six, Nine and Fourteen Years after Operation by the Laryngo-fissure Route.—Sir STCLAIR THOMSON, M.D.

(I) *Subglottic epithelioma, involving all one cord and the anterior third of the other. Division of the cricoid cartilage. No recurrence fourteen years after operation.*

Mr. W. F., referred in November, 1915, by Mr. A. J. Hutchison, who had diagnosed a subglottic malignant growth. Both cords were mobile. The growth extended from vocal process of left cord, forward to the commissure, which it crossed to invade anterior third of opposite cord. It descended so far in the subglottic space that the cricoid cartilage had to be split in the middle line so as to peel the growth from its inner surface. Fifteen months afterwards the patient returned with a malignant cervical gland, which was removed. There has been no recurrence either in glands or larynx. He has a useful voice, and, until recently, he has enjoyed what he himself describes as "excellent health," at the age of 73 and fourteen years after operation.

Mr. Colledge grades the malignancy in Group III. This high degree of malignancy is interesting in view of the fact that recurrence took place in the glands fifteen months later. As regards freedom of the larynx from recurrence, the examination of the sections made in the three usual sites warranted Dr. C. Fletcher (who reported on my specimens during many years) in stating as follows: "Excision is clear above, below and behind; the cancer cells penetrate deeply into the substance of the cord reaching down to the muscles. In one spot the cancer cells are to be seen very near to the line of excision, and, though there is no actual evidence that the excision is not deep enough, this must be regarded as the only doubtful point. Anteriorly, the epithelioma has spread to the opposite (right) cord, but excision is clear above, below and behind." We may conclude that though malignancy was marked, and that though the disease involved all one cord, part of the other and the subglottic area down to inside the cricoid—yet complete excision had been effected by the laryngo-fissure route and a lasting cure effected.

(II) *Subglottic cancer, invading anterior two-thirds of cord. Good mobility. No recurrence eight years and nine months afterwards.*

A solicitor, aged 60, referred in February, 1921, by Mr. Musgrave Woodman, who had performed a biopsy and made the diagnosis. At operation we found that the irregular infiltration of the anterior two-thirds of the right cord was an upward extension of a typical, anterior, subglottic cancer. The removal of the greater part of the thyroid ala facilitated the extension of the sub-perichondrial dissection to the inside of the cricoid ring. The tracheotomy tube was discontinued

after twenty-four hours. The patient was reading the evening newspaper the same day. Next day he was sitting out of bed and swallowing easily. The temperature chart shows the uninterrupted recovery.

A small portion of the opposite cord and subglottic tissue was also removed. In spite of this, the patient has a voice strong enough to carry on a large business. He has not been inspected for seven years and a half. His age is now 68.

The growth was reported by the late Professor Shattock, whose experience was unique in this department, to be "a squamous-celled carcinoma of a low grade of malignancy."

Mr. L. Colledge (who had not been informed of this report) graded the removed neoplasm as Group II. This is interesting, as Dr. C. Fletcher, after examining sections from all the removed mass, reported "the margin of uninvaded tissue, exteriorly and anteriorly, was extremely small and that he would consider recurrence likely in this case."

There has been no recurrence in eight years and nine months.

(III) *History of voice trouble for five or, possibly, thirteen years; misleading report from biopsy; large subglottic epithelioma. Laryngo-fissure exposing inner surface of cricoid. No recurrence and good voice six years later.*

Mrs. H., physician's widow, referred by Mr. F. H. Westmacott in 1923. Then aged 50. Gave a history of being "husky" in 1910, of having been kept on silence for two months, and of having taken a trip to the Canary Islands for the benefit of her voice. In 1918, pink polyp seen on anterior portion of left cord. Removed under suspension laryngoscopy August, 1922. Pathologist's report: "A small portion of the epithelium shows irregular hyperplasia, not enough to enable us to decide whether this is the beginning of a malignant growth, but we think it is probably not."

First seen by me a year later (i.e., July, 1923) as "the papilloma had recurred and required removal." The note I then made was as follows:—

"The whole left cord is pink and beefy, as if infiltrated with a growth from below. The margin is serrated. Below this, in the subglottic space, is a typical, grey, cupped growth. The cord moves freely, but flags in the anterior third. The epiglottis, ventricular band and arytænoid are not invaded."

The report entered was:—

"Epithelioma, for which a laryngo-fissure may be tried, although in view of the long history (five years since lesion of cord first detected), extension to whole cord and large subglottic growth, the prognosis is not good."

At operation (August 3, 1923) Dr. Gabriel Tucker (Philadelphia) and Mr. L. Colledge assisted. Growth typically subglottic, with cupped centre and raised margin, upper border of which just involved edge of cord, along which it extended backwards to the vocal process. Great care was required in peeling growth off inner surface of cricoid. It was removed, intact and *en masse*, with a good margin in all directions. Only little bleeding, so tracheotomy tube was abandoned at conclusion of operation, but had to be replaced, a week later, owing to suffocative attacks due to a sloughy condition along inner margin of the cricoid. Tube discontinued after a week and patient returned to the country twenty-five days after the operation.

Has remained in excellent laryngeal health. Uses voice naturally and freely and it is surprisingly good, when it is noticed that there is some web formation on the right (the sound) side. This is due to the fact that the thyroid cartilage was split a little to the right of the commissure, so as to ensure a good margin anteriorly. A little scar tissue can be seen in the endocricoid region, but there is no stenosis.

Pathologist's Report.—"An undoubted epithelioma, forming an elevated tumour the size of a sixpenny piece. The growth passes down and amongst the muscle planes with much surrounding small-celled reaction in the depths. Excision is complete in all directions" (G. L. Eastes).

Mr. L. Colledge considers that the malignancy should be graded in Group III. It is noteworthy that though he puts the degree of malignancy so high, yet examination of the slides in the three usual sites showed "excision complete in all directions," and it is doubtless due to this that there is a lasting cure.

(IV) *Subglottic cancer with impaired mobility of anterior half of cord. Diseased area removed* en masse (*Specimen shown*). *Remarkably good voice and no recurrence after four years.*—A gentleman, aged 59, referred in 1925 by Mr. F. Wrigley, who had diagnosed the condition and noted that "the movement of the cord was slightly impaired." The anterior two-thirds of the left cord was "occupied by a red, infiltrating, slightly cupped growth, extending forwards close to the anterior commissure and downwards on the inner margin." The opinion was given that the case was "suitable for removal of the growth by the laryngo-fissure route, but with the reserve that the growth might be found to have crossed the anterior commissure or descended far into the subglottic area. In that case careful watch should be kept for a recurrence and then promptly operated on."

Drs. Chevalier Jackson, Dean, Sutherland (U.S.A.), and Gavin Young were present at the operation. The larynx was inspected a few days later by Drs. Birkett, Robertson (Brisbane), J. W. Mackenzie (Inverness) and Gardères (Pau).

At the operation a typical growth was found descending half an inch below the cord, but stopping short of the anterior commissure. The removal of the thyroid ala facilitated the dissection from the inner surface of the cricoid ring. The tracheotomy tube was left in for only nine hours.

The patient was sitting out of bed and swallowing solid food on the fifth day.

Discussion.—Dr. LOGAN TURNER, commenting on the fact that in one of Sir James Dundas-Grant's cases (see p. 24) and in one of Sir StClair Thomson's, the patient was a woman, said that he had recently heard an interesting paper by the Registrar-General for Scotland on the alleged causes of the increase of cancer. From the death-certificate records three periods were reviewed (1911, 1921, 1928) showing a definite progressive increase. It seemed clear, however, that the increase was apparent rather than real, being based first, on a more accurate and early recognition of the disease, and secondly, upon the greater longevity of people at the present time. There seemed, further, to be an increase of cancer of the larynx in women. Sir StClair Thomson had stated that in recent years he had seen more cases of cancer in women than formerly. At the discussion on the paper referred to, he (the speaker) had raised the question whether some of the deaths certified as being due to cancer of the larynx in women might not have been due to a secondary infiltration, the primary disease having been in the post-cricoid region, which in the female was a common area for primary carcinoma.

Dr. A. J. HUTCHISON said he regretted that the patient whom he sent to Sir StClair Thomson in 1915 had been unable to attend this meeting. Two other patients sent to Sir StClair and operated on by him in 1917 had died last year without any recurrence of the growths. One of these had had huskiness for only eight weeks before the operation. A few weeks before he died, aged 79, he had written saying that there had been no delicacy in the throat since the operation, that he went out in all weathers, and that in February, 1928, he had addressed a meeting of one hundred people and had been well heard.

The other had had huskiness for six months before the operation. He died suddenly, aged 85, from fatty degeneration of the heart. His son had written saying that the old man had enjoyed life up to his last hour.

The PRESIDENT said he had always had the impression that it was unwise to treat subglottic growths through a laryngo-fissure, but the cases shown to-day would lead to a revision of these ideas. Sir StClair Thomson seemed to be leaving his old love, laryngo-fissure, for he had done what amounted to a hemi-laryngectomy in some of these cases. Removing a portion of the thyroid cartilege and doing ordinary laryngo-fissure seemed to be another departure. The drawback of hemi-laryngectomy in the old days was that the cases were liable to become septic. That was less likely in laryngo-fissure. He asked what were Sir StClair's reasons for extending his operation in this direction.

Sir. StClair Thomson, in reply, dealing with the question of the greater frequency of occurrence of cancer in women, said that of seventy cases treated by laryngo-fissure, sixty were in men and ten in women, those in women being at an earlier stage of life. In none of the ten women was the growth a secondary cancer; it was always primary in the larynx. As to predisposing causes, none of the ten women either smoked or drank spirits. Subglottic cancer was much more serious than pure cord cancer, and it was not even favourable for complete laryngectomy. In more than half the subglottic cases he had operated upon the condition had recurred, whereas among his cases taken as a whole the successes were 78%, and the pure cord cases 84% of lasting cures. It was worth while trying to remove the growth in subglottic cases, but it must be realized how deep one might have to go. Operations had advanced a good deal since the larynx was opened and the cord simply clipped out. In the last forty cases he had not only raised the diseased area on its perichondrium, but he had taken out the thyroid ala. Hemi-laryngectomy of former days was rightly looked upon as more fatal than complete laryngectomy. As the President had remarked, the technique of the operation known as "a laryngo-fissure" had been developed until now it was practically a hemi-laryngectomy, done through a thyrotomy from the inside.

Fibrous Stricture of the Œsophagus caused by Swallowing Lysol Five Years Ago. (Skiagrams shown.)—Archer Ryland, F.R.C.S.Ed.—R. P., a girl aged 9, first seen by me five years ago, when she was admitted to hospital on account of difficulty in swallowing, following the accidental taking of lysol by mouth. Skiagrams at this time showed the formation of a long, narrow stricture about the middle of the œsophagus.

Treatment by gradual dilatation by means of the œsophagoscope was carried out and maintained over a period of months. During the last five years the child has been lost sight of until a few days ago, when she was admitted to the Central London Throat Hospital with a history of having swallowed a plum stone, which was presumed to be impacted in the œsophagus. Skiagram and œsophagoscopy excluded the presence of a foreign body.

The case is now brought forward to show the state of this fibrous stricture, five years after its formation. The child is on ordinary diet and is "eating well." It will be noticed that, for her age, she is small, puny and under-developed.

Tumour of Naso-pharynx.—J. D. McLaggan, F.R.C.S.—J. B., male, aged 21. *History.*—Seen at Central London Throat Hospital, November 16, 1929. Complained of nasal obstruction and post-nasal discharge of about nine years' duration.

Examination shows a tumour in the naso-pharynx, situated on the roof and posterior wall, oval in shape, and of the size of a grape. It is covered with smooth epithelium, and is elastic in consistency. There is also an œdematous swelling on the left side of the septum. Provisional diagnosis, lipoma.

Enchondroma of Larynx.—Dan McKenzie, M.D.—The patient, a woman, aged 61, has been under observation during the last three or four years. There are no laryngeal symptoms, and the tumour was discovered accidentally.

It forms a smooth prominence below the left vocal cord, extending not quite to the middle line. Direct examination shows it to be hard to the touch. During the time it has been under observation it has not shown any increase in size. It is evidently growing from the cricoid cartilage.

Dr. Douglas Guthrie said that he had on two occasions observed, in men past middle age, a well-marked prominence on the cricoid cartilage just below the anterior commissure. Was it possible that abnormalities of chondrification accounted for such an appearance, apart from the presence of an actual tumour, which might be styled chondroma?

Osteoma of the Frontal Sinus. Operation for Removal.—L. Graham Brown, F.R.C.S.—L. B., male, aged 34, referred from an ophthalmic hospital, complaining of intermittent pain over left eye, of fourteen days' duration. Tenderness over left frontal sinus. Rhinoscopic examination negative.

Skiagram (shown) suggested an osteoma growing from the floor of a very large sinus.

Operation.—Diagnosis confirmed. Removal of bony growth with part of the floor of the frontal sinus. Creamy pus evacuated from the supra-orbital portion of the sinus, distal to the growth. Wound treated by the open method closed completely in a fortnight. Sinus now apparently functioning normally.

[Mr. Graham Brown showed a second skiagram of an apparently similar condition discovered accidentally in another patient. This, up to the present, had not given rise to any symptoms.]

Mr. HERBERT TILLEY said that many years ago he had operated upon an osteoma of the fronto-ethmoidal region in Edinburgh, where he had the advantage of being assisted by Sir Harold Stiles. He (the speaker) made an external incision, opened the frontal sinus and exposed the upper part of the tumour, but grasped the lower part with forceps inserted into the right nasal cavity. The growth was loosened and drawn downwards and the problem was, having got it into the nasal cavity, how to deliver it through the nostril. Sir Harold Stiles then gave him a hint which he had since found useful in cases of large growths inside the nose, such as fibromata. If one cut through the whole length of the lower attachment of the septal cartilage the delivery of a tumour was much easier than otherwise. That had been done in the case referred to; the osteoma was removed without difficulty.

Laryngeal Growth. Case for Diagnosis.—L. GRAHAM BROWN, F.R.C.S.

B. S., male, aged 51, first seen November 19, 1929, complaining of hoarseness and occasional left earache for the past four years. The larynx shows a large, irregular ulcerated growth occupying the region of the left vocal cord and extending to the anterior third of the right cord. No immobility apparent. Chronic suppuration of the left middle ear. Wassermann reaction of blood negative, though patient states that, when in the Navy thirty years ago, he contracted syphilis for which he received appropriate treatment.

The tentative diagnosis of epithelioma is put forward, the result of bioscopy not yet being available. An intraspinal-fluid examination is also being undertaken.

Discussion.—Dr. P. WATSON-WILLIAMS said it was an open question whether the long previous syphilis had anything to do with this condition, which sometimes occurred when there was no history of syphilitic infection, and which he thought was best described as a pachydermia diffusa. He had watched such a case many years; it looked remarkably like the present one, and at first it had caused a good deal of anxiety. There was, however, nothing malignant about these cases, though he supposed they might possibly become so in course of time and should be under observation at intervals.

Mr. ALEX. R. TWEEDIE said that he had been unable to obtain approximation of the cords on phonation and noted that with the glottis still wide open the stridor was unaltered.

Mr. H. TILLEY said he thought there was a definite and extensive ulceration of the left vocal cord, involving the ventricular band, and he would regard the condition as epithelioma.

Dr. JOBSON HORNE said that whilst admitting that the case presented points of difficulty in diagnosis, he considered that it could not be regarded as pachydermia laryngis verrucosa, the history of syphilis might suggest pachydermia laryngis diffusa syphilitica.

In pachydermia the mucosa was thickened but intact: in the present case there was evidence of ulceration. In pachydermia there was no impairment of the mobility of the vocal cords; in the present case there was impaired adduction of the vocal cords. Lastly, pachydermia laryngis did not become malignant: in the present case there were points suggestive of malignant disease.

Mr. E. WATSON-WILLIAMS said that he had seen a number of cases similar to this, of which only two or three were comparable in degree: they had all occurred in patients who had had syphilis, which was no longer active. He regarded the condition as a hyperplastic laryngitis of syphilitic origin. One of his cases he had been able to watch for three years, during which time it had remained practically stationary; there were horns on

one cord, on the other, recesses into which these fitted, and bosses and knobs on the arytenoids and in the inter-arytenoid space. He did not think there was any suggestion of malignancy in the present case.

Mr. ANDREW WYLIE said he did not see any ulceration in this case; he regarded the condition as pachydermia. It would be easy to settle the diagnosis, however, by removing two or three pieces for microscopic examination. The patient had had the disease four years, and if it was malignant, the condition would be far worse than it is at present.

Mr. H. V. FORSTER said he thought he saw, far out on the right ventricular band, well away from the main amount of overgrowth, a separate nodule, looking like a discrete papilloma.

Sir STCLAIR THOMSON said that Dr. Jobson Horne was positive that the condition was not pachydermia, and he (the speaker) felt equally positive that it was not malignant disease, though admittedly it might become so. The right cord was absolutely fixed, and the left was nearly fixed. Between them there was a great inter-arytenoid irregular hypertrophy. It looked quiet and non-ulcerated. This reminded him very much of what he saw before the days of the Wassermann test and before treatment by salvarsan, i.e., a parasyphilitic, hypertrophic laryngitis. He suggested that if this patient would entirely stop smoking, have his mouth properly cleaned, and then have inunction of mercury, his condition would be greatly improved, but he would never become well.

Sir JAMES DUNDAS-GRANT said he thought the condition was a warty growth in the ventricular band and inter-arytenoid space. It was probably the result of syphilis; he did not regard it as epithelioma. It was more like the condition which Virchow described as pachydermia verrucosa.

Mr. GRAHAM BROWN (in reply) said that his tentative diagnosis had been rather a hasty one. He now thought the condition was hypertrophic, and there was the possibility that it might become malignant. He felt that more active treatment was required than merely prohibiting smoking and ordering inunction of mercury.

Two Cases of Spontaneous Hæmorrhage into the Fossæ of Inflamed Tonsils.—V. E. NEGUS, M.S.

(I) Patient, male, aged 47. Referred by Dr. J. S. Rogers (Farningham).

October 22, 1929.—Acute tonsillitis. One week later, appearances of quinsy on right side. Opening made; nothing except blood followed the incision. Improved for the next week.

November 8.—Had severe hæmorrhage twice; thinks he lost a pint of blood. Hæmoplastin, 2 c.c. given, and at the request of Dr. Rogers the patient was taken into King's College Hospital. Hæmorrhage had then ceased. Patient rather pale but general condition good. Blood-count showed: Red cells 4,000,000, hæmoglobin 73%. On the second day after admission (November 10) he had two small hæmorrhages and one large one. Blood seen to ooze from upper pole of tonsil and also from a crypt towards lower end. None oozing from incision in palate. As the blood appeared to be from tonsillar vessels, it was necessary to remove the tonsil. As soon as the anæsthetic was given, blood poured from the tonsil and filled the mouth and pharynx. After clearing this away the tonsil was removed, and appeared friable, resembling a new growth. Outside the capsule there was a large cavity containing some fresh blood and many clots. This was cleared out and no more bleeding was seen. A large pack was sewn in, the two pillars of the fauces being united over it. The red cells had fallen to 3,440,000 and the hæmoglobin to 54%.

Transfusion was carried out (Group IV, 600 c.c.); patient improved rapidly. Pack was taken out two days later, and there was no further hæmorrhage. When he left hospital two weeks after admission (November 21) blood-count showed red cells 4,680,000, hæmoglobin 65%. Report by Dr. Creed stated that the section of tonsil removed showed evidence of fibrosis and acute inflammation. Some parts showed infiltration with polymorphonuclears, and plasma cells were very numerous in other places.

(II) Boy, aged 13½. Referred by Dr. Bland, June, 1927. History of fever, vomiting, rhinitis with some epistaxis, swelling of glands in the neck, and inflammation of pharynx. Swab showed pneumococci only. Tonsils had been removed previously.

When first seen by me ten days after commencement of illness, glands below angle of jaw on right side were enlarged, there was considerable swelling of right side of pharnyx and naso-pharyngeal wall, with enlargement of tonsillar remains. Two days later, patient had two small hæmorrhages and one larger one, a cupful of blood being expectorated. When seen he had great pain and marked swelling of palate with all appearances of quinsy. Incision made in ordinary position, but instead of discharge of pus, blood poured from the opening made, filling two kidney dishes. Bleeding was stopped by firm pressure with the finger. The bleeding was so free that it appeared as though a branch of the external carotid artery had burst into a peri-tonsillar abscess, and it was thought necessary to tie that vessel. Mr. Dunhill arrived with Dr. Langton Hewer, who gave the anæsthetic. As soon as the anæsthetic was administered the wall of the pharynx burst and blood filled the mouth, pharynx and trachea. The patient became cyanosed and tracheotomy was performed. Blood was swabbed out and the external carotid was exposed. The superior thyroid and lingual arteries came off separately and were tied, but bleeding continued. The external carotid was tied higher up. Bleeding ceased.

Because of œdema of the pharynx, the tracheotomy tube had to be left in. Patient progressed well for one week; there was paralysis of the right side of the tongue. On the seventh day he awoke from sleep, had a sudden violent hæmorrhage, and bled to death in a minute or two.

Post-mortem examination showed a large sloughing inflammatory cavity lying under cover of the angle of the mandible and containing some pus and blood outside the pharynx, extending up to the base of the skull. The ascending pharyngeal artery appeared to go through the cavity and to have burst. The hypoglossal nerve was found to run through the cavity. There was early pneumonia in both lungs.

Discussion.—Mr. H. BELL TAWSE said that a more suitable title for the first case would be "Secondary hæmorrhage after incision of a quinsy." An incision had been made in the palate ten days before Mr. Negus saw the case and possibly a small vessel was injured and additional sepsis introduced then, thus providing the two principal factors necessary for a secondary hæmorrhage. Moreover, secondary hæmorrhage after a tonsillectomy usually occurred about nine days after operation. That the blood did not come out through the palatal incision did not negative his argument. The blood followed the line of least resistance through a crypt. In such a case he suggested that one should immediately ligature the external carotid and deal with the tonsil then or later; this would obviate the necessity for plugging the septic tonsillar cavity and stitching the faucial pillars over it, a proceeding which he disliked as tending to produce secondary hæmorrhage. In secondary hæmorrhage elsewhere one ligatured the main vessel well away from the septic wound and drained the latter. In the second case, Mr. Negus had tied the external carotid twice, but he did not state whether he ligatured below the origin of the ascending pharyngeal artery. This was an important point, as at the post-mortem examination the ascending pharyngeal was found ruptured in the middle of the abscess cavity. In April, 1929, he (the speaker) had reported a case[1] of spontaneous hæmorrhage from the right tonsil. The patient was a man who had had frequent quinsies for twenty years, but they always burst and no attempt had been made to incise them. On this occasion he had been ill for a fortnight and a quinsy on each side appeared to be on the point of bursting, when without any warning blood gushed out of his mouth and he rapidly lost five pints. A week later three more pints of blood came from the right tonsil and he nearly died. He had had syphilis in his younger days, and although his Wassermann reaction had been repeatedly negative, the possibility of a deep-seated gumma could not be ruled out. A ligature was put round the common carotid and left untied. The pharynx was constantly under inspection, whilst the external carotid was ligatured so that a sudden hæmorrhage could be immediately controlled. For over a week a nurse was at his

[1] *Journ. of Laryng and Otol.*, 1929, xliv, 257.

bedside night and day ready to apply traction to the common carotid ligature, and on the tenth day the ligature was removed. An interesting point was that within twenty-four hours the pain had left the right tonsil which had shrunk to one-half its former size, whilst in the other tonsil an abscess formed and was opened. Two months later the tonsils were dissected out with the greatest difficulty from a bed of scar tissue. These cases should always be regarded as serious. Many of them were fatal; he had known a patient die from hæmorrhage during the induction of anæsthesia. They should be treated as cases of secondary hæmorrhage, by ligature at a distance, and not as cases of primary hæmorrhage, by ligature of the bleeding point in the midst of an inflamed and septic area.

Mr. A. J. WRIGHT said that some years ago a patient had repeated secondary hæmorrhages following spontaneous rupture of a quinsy. He was brought from the country on an ambulance, and when he (the speaker) first saw him he was white from loss of blood. However, after removing the tonsil, he (Mr. Wright) controlled the bleeding at the site, and the patient recovered. Ligation at a distance from the bleeding point should be reserved for cases in which attempts at the site were unsuccessful.

Mr. E. WATSON-WILLIAMS said that an article by Mayer in the *Wiener Klinische Wochenschrift*, in April, 1926, might have been written to illustrate these two cases. In the first part the ordinary quinsy was discussed and mention made of severe hæmorrhage following the usual incision; a case was described where excision of the tonsil was adopted to control the bleeding. The second part dealt with a second type of peritonsillar abscess, which he (the speaker) preferred to call parapharyngeal; the pus collected not in immediate relation to the tonsil, but behind the palato-pharyngeus, in the substance of, or, outside the pharyngeal wall. Mayer laid emphasis on the danger of pus travelling down the carotid sheath, and of the possibility of arterial erosion; he advocated external opening and drainage. He (the speaker) found that this type was not very rare; he had met with eleven cases. Clinically they resembled quinsy, but without the œdema of the uvula which was seldom lacking in the latter condition. It was easy to open the abscess when one was on the look-out for it, behind the lower pole of the tonsil; a blunt instrument was quite sufficient as there was only unsupported mucous membrane to divide; he himself had done this with the tip of his finger, and in his last case with a tongue-depressor. The abscess tended to point in the lateral wall of the pharynx.

Mr. F. C. CAPPS said he had had a similar case three weeks ago. The patient, a woman, aged 25, had come to hospital after having had a fortnight's treatment for tonsillitis. As she seemed better, her doctor allowed her to get up. Bleeding had begun suddenly, and when he (the speaker) saw her was still continuing. In her case there had been no opening of a quinsy or any surgical treatment. The bleeding was from an upper crypt in the left tonsil and in hospital the patient vomited another pint of bright blood. He decided it was better to stop the bleeding at the site. He removed the tonsil, but it was difficult to do so owing to the recent inflammation of the pillars. The whole fell away as a friable mass, and beneath was a clot the size of a damson. When this was cleared out, a free space was left in the tonsillar fossa and he plugged it with bipp gauze. There seemed to be no sepsis. The plug was removed in three days, and recovery was uninterrupted.

Mr. BROUGHTON BARNES said he had had a case of hæmorrhage on the fifth day after a quinsy was opened. He saw the patient fifteen minutes after the beginning of the free hæmorrhage; he had then brought up half a pint of blood, which was coming from the quinsy opening. He enlarged the opening, and packed it with iodoform gauze, taking out the plug in twenty-four hours. Bleeding did not occur again for twelve hours, and then there was a small hæmorrhage. He repeated the procedure and there was no further trouble.

Mr. NEGUS (in reply) said the doctor who had opened this abscess was afraid he had caused the trouble, but he (the speaker) had tried to reassure him by telling him of the earlier case in which no incision had been made. It was not necessary to think that the operation had infected the peritonsillar space, as the infection was already there. This patient had quinsy, which was sufficient to cause sloughing, but in some cases further infection might have been carried in. In the earlier case there had been no operation, and therefore the sloughing was from sepsis which had travelled outside the tonsil. He did not himself tie the carotid, because he was concerned with controlling the bleeding in the pharynx. The

superior thyroid and lingual arteries came off separately. When the external carotid was tied, the bleeding ceased. As the bleeding came on again a week later and the boy bled to death, the tying of the carotid was not very satisfactory, first, because of the wide anastomosis with the opposite side, which was established after a few hours, and secondly, because then the bleeding might be venous as well as arterial. Therefore controlling the bleeding in the tonsillar fossa seemed to be better, when practicable. In the case of the boy the area involved had been too widespread for this to be done.

He never put in a pack after tonsillectomy, but, in this case, having taken out the tonsil, the whole tonsillar fossa was laid bare and there was no arterial bleeding, and therefore the only way to control the bleeding was to put in a pack. He soaked it in protargol.

Mr. Wright had said that controlling the bleeding at the site was preferable, because anastomosis on the opposite side was dealt with then, as also bleeding from veins.

Mr. Watson-Williams's suggestion might be correct for such cases as the earlier one, but it would not have been correct for the patient shown at this meeting, as in his case the blood was between the superior constrictor and the capsule of the tonsil.

A Radium-Needle Introducer for Use in the Hypopharynx.—D. A. CROW, M.B.

Whilst the simpler forms of introducer are convenient enough for the middle pharynx, I have felt the need of an instrument such as this which gives an accurate aim and is slender enough to be used through a direct laryngoscope on epiglottic or other circumlaryngeal growths. To avoid damage to the silk thread, movements must be slow and gentle.

A longer instrument on the same principle might be used for œsophageal growths, but it is felt that some method of intubation is preferable, where the presence of a stricture makes access to the lower part of a growth difficult.

One advantage is that it does not make a bigger hole in the tissues than the diameter of the needle. That is the difficulty with some introducers which are themselves plunged some distance into the tissues. The trouble is not in planting them in, but retaining them there.

Mr. NORMAN PATTERSON said that a needle with a barbed end stayed in position better than one with an ordinary point. On his suggestion, self-retaining radon needles had been manufactured.

Carcinoma of Tongue and Floor of Mouth.—NORMAN PATTERSON, F.R.C.S.

Male, aged 54. Two years ago noticed something in the right side of the floor of the mouth which felt like a crumb. Last six months at times intense pain which shoots to the tip of the tongue and sometimes spreads to the right ear. No loss of weight, appetite good. Ulcer has been cauterized on three occasions; on one the actual cautery was employed. Wassermann reaction negative. The case was sent to me with a provisional diagnosis of lupus, an opinion with which I do not agree.

On Examination: Tongue protruded to right of middle line and cannot be pushed beyond the lips. Superficial ulcer on right side of tongue with irregular edge, which bleeds on probing. Ulcer extends to floor of mouth and on to alveolar margin, and anterior pillar of fauces, where the condition is more granular in appearance. Some swelling of posterior third of tongue on right side. On palpation, right side of tongue is firm; rolled edge on anterior faucial pillar. Hard swelling in the right digastric triangle, which patient states has been present for about two months.

Microscopical examination confirms the diagnosis of carcinoma.

Lymphadenoma, with Involvement of the Larynx.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

Patient, male, aged about 38. Complained of huskiness, of six months' duration. Appearance of larynx: Fleshy infiltration of aryepiglottic folds and, to a lesser degree, of epiglottis; infiltration of left vocal cord with ulceration along the edge; infiltration of right vocal cord. No tubercle bacilli found in sputum after three examinations. X-ray examination of chest negative. In May, 1928, gland removed

from right axilla and right side of neck—reported to be lymphadenoma. Has had treatment by means of X-rays, sometimes three times a week, sometimes twice. Patient says that the hoarseness came on after X-ray treatment of neck.

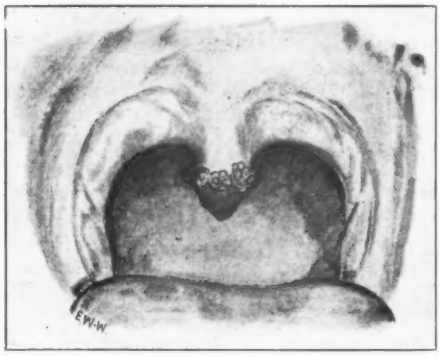
He says that he has felt much better and that swallowing has been easier since he began to take iodide of potassium (5 gr., three times a day).

Discussion.—Mr. HAROLD BARWELL asked whether the appearance was now the same as before the irradiation. He did not think that œdema of the larynx was common in lymphadenoma, and he wondered how much of what was seen was due to the irradiation.

The PRESIDENT said the relationship of lymphadenoma to the region of the laryngologist was interesting. He used to think this disease always began in the tonsils, and that infection reached the glands by way of the tonsils, but he had recently seen a case of the kind in which the disease definitely began in the mediastinal glands, the neck glands and tonsils being unaffected.

Specimen showing Carcinoma of the Uvula removed at Operation from a Patient aged 80.—E. WATSON-WILLIAMS, M.C., F.R.C.S.Ed.

A. T., male, aged 80, consulted me, July, 1927, complaining of pain in the throat, worse on swallowing, for about one month. No other relevant history. On examination, I found a papillomatous mass at the end of the uvula, ulcerated in



the centre. I considered this probably malignant, and during the ensuing fortnight the edge advanced visibly up the uvula, the ulceration following, so that the tip of the uvula presented a blunt red cone emerging from a collar of papillary growth. The mass was very tender, and hard, and bled readily. No glands felt.

Owing to age and arteriosclerosis a severe operation or even a general anæsthetic were considered inadvisable; under local anæsthesia I removed the uvula, with a small area of soft palate [shown]. The wound healed well, and the patient remained in good health for nearly two years. In July last he died from cardio-vascular disease, having had no recurrence of the growth.

This appears to be one of the growths of relatively low malignancy, not rare in the aged. The section shown is that of typical epithelioma, infiltrating the muscle tissue.

Epithelioma: Patient Well after Treatment ten years and eleven months ago.—NORMAN PATTERSON, F.R.C.S.

Male, aged 71. Early in January, 1919, was sent to London Hospital complaining of pain on swallowing.

On Examination : Large epithelioma involving nearly whole of right half of soft palate, crossing middle line as far as left side of base of uvula and extending downwards on right anterior pillar of fauces to the tongue. The tumour extended forwards nearly as far as the junction of the hard and soft palate.

On January 6, 1919, diathermy was applied. On February 2, 1919, a complete block dissection including the removal of the sterno-mastoid and internal jugular vein was carried out on the right side. It is now ten years and eleven months since the diathermy, and the patient still remains well.

Microscopic report: "Squamous-celled carcinoma."

Discussion.—The PRESIDENT: The question as between radium and diathermy will be settled by the survival factor. What method cures most cases? It is that method which will survive. These were admirable cases of Mr. Patterson and showed what could be done by diathermy.

Sir JAMES DUNDAS-GRANT said this was a more promising case than any he himself had had. In a case of epithelioma of the uvula which he had treated with diathermy, the result for the time was perfect, except that air came through his nose, but eventually there was a recurrence.

Mr. NORMAN PATTERSON (in reply) said that the patient thoroughly recovered, and he drove a railway express train for five years after the operative treatment. He then retired at the usual age, and still remained a useful member of the community.

Swelling above Right Vocal Cord; Outgrowth on Left Vocal Cord. Case for Diagnosis.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

Patient, male, aged about 70. Singer in a synagogue. Complained of hoarseness of three months' duration. Appearance of larynx: large rounded swelling above right vocal cord; irregular sessile outgrowth on left vocal cord. No tubercle bacilli in sputum. Wassermann reaction negative.

[Microscopic examination showed chronic inflammatory changes in sub-epithelial tissues and hyperplasia of epithelium—non-malignant.]

Mr. HAROLD KISCH said that this patient went round from one hospital to another. His (Mr. Kisch's) own diagnosis when he saw the man had been papillomata of the larynx, on the strength of which operation had been performed in Germany some years ago, and a good deal of the cord had been taken away. He (the speaker) removed a portion and found that it was papilloma There was no sign of malignancy.

A Chromium-plated Head Mirror.—D. A. CROW, M.B.

This has the advantage of being non-breakable and yet gives as bright a reflection as the ordinary silvered glass.

Modification of the Davis Gag.—J. C. CLAYTON, L.R.C.P., M.R.C.S. (introduced by HAROLD KISCH, F.R.C.S.).

This modification in no way alters the general principle of the gag, but, by an easily-worked contrivance, different dental pieces can be fixed to suit different mouths.

Further Reports of Three Cases previously Shown.

Reticulo-Sarcoma, formerly Left Tonsillar region, lately Right Tonsillar region (shown June, 1928)[1]. Radium Treatment. Recovery.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.—Male, aged 64. In March, 1928, extensive invasion of left tonsil, and root of tongue, "grubbed-out" in pieces. Tube containing 25 mgm. of radium sewn into the cavity by Mr. Cole; retained twenty-four hours. Parts clear when previously shown.

[1] *Proceedings*, 1928, xxi, 1798 (Sect. Laryng., 100).

Further growth on left half of epiglottis, causing pain and difficulty in swallowing, removed by Goughenheim's punch forceps. Later, enlargement of right tonsil, enucleation followed by recurrence in right tonsillar region and then enlargement of glands of neck on both sides.

July, 1929, insertion of radium into tonsillar growth on right side, 1020 millicurie hours. Rapid diminution of the tonsillar growth. Surface application of radium to glands on right side, followed by considerable diminution. Later, distance irradiation to glands on left side with "bomb"—36 grm. hours—great diminution in size of glands.

At present no abnormality except a defect in left half of epiglottis from operation with punch forceps.

Epithelioma of the Larynx: Laryngectomy (shown November, 1923).[1]—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.—Female, aged 35. Complete laryngectomy over six years ago. No recurrence. Good health. Microscopical section and specimen. The case is a contradiction of the ideas which used to be expressed, that subjects of laryngectomy were so miserable that their life was worse than death. This patient is exceptionally cheerful.

(?) Localized Hodgkin's Disease. Case for diagnosis. Previously shown as a case of Tonsillar Tumour, November 2, 1928.[2]—LESLIE POWELL, M.B.—Patient seen again, August 27, 1929. For three months had had swelling of glands of neck on left side, no pain; feels well. The pharynx is perfectly healed. The glands are soft, discrete and smooth, forming a considerable swelling without signs of inflammation or breaking down. They extend down to the clavicle. The axilla is clear, and there are no glands palpable elsewhere. This I think confirms the suggested diagnosis of localized Hodgkin's disease. The patient has since been treated with arsenic, and the glands have considerably diminished in size.

[1] *Proceedings*, 1923, xvii (Sect. Laryng., 5).

[2] *Ibid.*, 1928, xxii (Sect. Laryng., 7).

Section of Neurology.

CASES SHOWN AT THE CLINICAL MEETING HELD AT THE WEST END HOSPITAL FOR DISEASES OF THE NERVOUS SYSTEM, WELBECK STREET, W. 1, JANUARY 9, 1930.

Periodic Paralysis.—E. D. MACNAMARA, M.D.

W. W. M., aged 62. Grave-digger. At the end of 1913 suffered from ophthalmoplegia and paresis of the arms. By the end of March 1914, was well, except for slight ptosis of left eyelid and some weakness of right external rectus. The patient had had a venereal sore in 1887, but his Wassermann reaction was negative in 1913. Similar attacks occurred in 1915 and 1918. In 1924 partial ophthalmoplegia again developed, with difficulty in holding objects, walking and swallowing. July, 1925, no symptoms or signs. July, 1929, complained of mistiness of vision and weakness of right hand. Gradually ptosis and ophthalmoplegia developed, with difficulty in moving the jaws, inability to use hands for work, and inability to walk beyond a mile.

Condition on admission to West End Hospital, September 28, 1929.—Pupils normal; retinæ normal. Right and left ptosis and considerable impairment of movements of each eye. Great weakness in grip of both hands. Able to walk short distances, with a tendency to drag his toes. Since then has considerably improved, but some degree of ophthalmoplegia persists and hand-grips are not strong. Wassermann reaction negative, both in blood and in cerebrospinal fluid.

December 7, 1929.—Small piece of the extensor carpi ulnaris removed. Dr. Carnegie Dickson reported that many muscle fibres showed patchy hyaline degeneration with swelling and coalescence of the fibrils and loss of their cross-striations. A few small groups of "lymphorrhages" were present.

Retinal Changes and Mental Retardation in a Member of a Family in which two cases of Schilder's Disease have occurred.—E. D. MACNAMARA, M.D.

Y. K., aged 2 years and 9 months.

Family History.—Elder sister was under care of Dr. Collier. Case fully reported in *Brain*, 1924, xlvii, 489. A second sister, aged 4 years and 11 months, has been under my care at the West End Hospital for Nervous Diseases (Schilder's disease). Brother aged 8, and sister aged 4, in good health.

Past History.—Y. K. was delivered by Cæsarean section. She was first seen by Dr. Mary K. Ruddy at an Infant Clinic, January, 1928. Was underweight, pale, flabby, and unable to sit up, and had a severe squint. When aged 16 months could not stand or walk and was not clean; could sit up and say a few words. At the age of 2 years and 5 months tried to stand but made no attempt to walk. Admitted to hospital August 2, 1929. Mental condition not equal to her years. Vision and hearing apparently normal. Strabismus present. Patient could not stand unless supported and walking was hesitating. Limbs apparently normal, though weak. Arm reflexes present. Patellar and ankle reflexes not elicited. Abdominal reflexes present. Plantar reflexes flexor. Mr. Lindsay Rea reports that the optic discs show atrophy and that the retinæ are peppered.

September 13, 1929.—Right facial paresis developed. This has almost completely cleared up. The mental condition has slightly improved. The patient is able to say a few more words and plays with toys and with other children in the ward.

The case is shown because of the family history and because, though it is not itself a typical case of Schilder's disease, the patient is evidently abnormal.

Myoclonus with Flaccid Palsy of the Legs.—E. D. MACNAMARA, M.D.

J. W., female, aged 2 years and 4 months. The mother's pregnancy and parturition were normal. J. W. began to walk at age of 14 months, and to talk at age of 6 months. She has had no illnesses. Six months ago went off her legs but was not otherwise ill. Her legs also began to "tremble."

Family History.—Nothing relevant.

On admission to the West End Hospital on November 15, 1929, her intelligence seemed normal. Cranial nerves normal. Could only stand with a good deal of support and no progression was possible. Legs were flaccid, reflexes all present, the plantars flexor. Clonic spasms of arms, trunk and head were frequent. Spasms of legs occurred less frequently. Blood and cerebrospinal fluid, negative. Patient can now only sit up with difficulty and does not move around in her cot. The spasms persist and occur in her sleep; she has become incontinent.

Chronic Hypertrophic Interstitial Neuritis.—C. WORSTER-DROUGHT, M.D.

R. W., a boy, aged 15, noticed weakness of grip in both hands fourteen months ago. Loss of power later involved both upper and lower limbs and back, and some numbness appeared in hands and feet. Condition has become steadily worse except that numbness disappeared seven months ago.

Was employed as a bookbinder's assistant, but the work did not entail the use of metal. Family history, negative.

Condition on Examination.—Mental state normal except for some delay in responses. Pupils and all cranial nerves normal; no definite sensory changes. Upper limbs: Hands held flexed at wrist and fingers; wasting general; weakness marked; tone diminished and deep reflexes absent; coördination good. Lower limbs: Loss of power most evident in anterior tibial and peroneal muscle groups; wasting general, tone diminished; deep reflexes absent, plantar reflexes difficult to obtain and usually flexor. Patient walks unsteadily but coördination is good.

Weakness of erector spinæ but not of anterior abdominal muscles. Abdominal reflexes cannot be elicited. Ulnar and external popliteal nerves definitely thickened, slightly irregular and hard to the touch but not tender.

Teeth are good and alveolar margins healthy. Remaining systems are normal.

Electrical Reactions.—Faradic response present in all muscles, and fairly easily obtained; galvanic reactions difficult to obtain but are brisk, a stronger current than the patient can easily tolerate is required to produce a contraction.

Cerebrospinal fluid was of normal appearance, contained 1 cell per c.mm., total protein 0·10%, globulin in slight excess, Wassermann reaction negative, Lange's test 1223321000. Blood Wassermann reaction negative, and a full blood-count normal. Blood-urea 47 mgm. per 100 c.c. Urine showed no abnormality.

Commentary.—The main question to be decided in this case is that of diagnosis. The condition present might be one of toxic polyneuritis in which the sensory fibres are involved only to a slight extent, the motor fibres bearing the brunt of the disease. If so, the ætiology is most obscure. On the other hand, the definitely thickened nerves strongly suggest a diagnosis of chronic hypertrophic interstitial neuritis (Dejerine-Sottas disease) in spite of the absence of family history and sensory and pupillary changes. Of the two, the latter appears the more probable diagnosis.

Myoclonia (for Diagnosis).—W. OGILVY REID, M.B. (introduced by W. R. REYNELL, M.D.).

G. R., male, aged 55, quite well until one year ago, when he began to be troubled with rhythmical trembling movements in both legs, more noticeable in left. Has gradually become worse. Movements at first were intermittent, but are now continuous, except when walking or asleep. He perspires a good deal after the trembling has been going on for some time. The condition is well controlled for

about four hours by hyoscine hydrobromide gr. $\frac{1}{150}$ by mouth. Patient can also stop trembling for about fifteen minutes when in bed, by placing left foot across dorsum of right foot and flexing both knees until thighs and calves are almost approximated. Trembling also tends to be inhibited by voluntary movement. Arms have never been affected.

Thyroidectomy five years ago; past history otherwise good.

Physical examination shows nothing abnormal in cranial nerves, upper extremities or trunk. Legs show rhythmical trembling movements. Slight wasting of both lower limbs, and tone is slightly increased. Deep reflexes increased; ankle clonus more pronounced on left side. Plantar response flexor. Attitude in standing and walking is one of slight flexion; he tires easily on walking. No abnormality in sensations, and no loss of sphincter control.

Recurrent Choreiform Movement Associated with a Residual Cerebral Lesion. ? Syphilis. ? Encephalitis.—NEILL HOBHOUSE, M.D.

G. B., a boy, aged 7 years and 11 months, has suffered from movements of limbs and face since he was aged $2\frac{1}{2}$. These have passed off at times, but have seldom been absent for more than a month or two. He has been to school very little, and has spent a large part of his life undergoing treatment for "chorea." Recently spent four months in an institution for rheumatic affections.

When seen on December 10, 1929, there was slight but definitely choreiform movement of both hands, mostly in the left. Attitude of left hand was slightly different from that of right.

Pupils almost inactive to light. Reflexes: Knee-jerk, right brisker than left. Ankle-jerks equal. Plantars flexor.

No evidence of rheumatism obtained.

Blood: Wassermann reaction, positive on December 12, 1929, negative on January, 1, 1930.

Cerebrospinal Fluid: Wassermann reaction, negative. Blood present; but probably no increase of cells or protein apart from this.

During the last fortnight the choreiform movement has grown much less. Mentally he is alert; he is ignorant, but his intelligence seems normal. He is talkative and inclined to be troublesome, but shows no definitely psychopathic traits.

Tabes with Charcot Knee and Normal Cerebrospinal Fluid.—NEILL HOBHOUSE, M.D.

F. M., aged 44. History of "rheumatics" for a few years, no other symptoms. The left knee has been swollen since 1917, but has given him no trouble. A well-marked case of tabes, with Argyll-Robertson pupils and absent deep reflexes in legs. No ataxia and scarcely any loss of sensation in limbs or trunk. The clinical and radiological features of the left knee suggest a Charcot's joint.

Cerebrospinal Fluid: Wassermann reaction, negative. Cells 1. Globulin nil. Protein 0·02%. Lange 0111100000.

The case appears to be unusual in that Charcot's joints are almost always associated with pathological cerebrospinal fluid, and usually with well-marked impairment of afferent functions.

? Recurrent Acute Internal Hydrocephalus of Idiopathic Origin.—Case for Diagnosis.—T. R. HILL, M.D.

J. D., female, aged 49. First seen August, 1929, when she complained of an illness which began in April, 1929, with insidious onset of headache and vomiting. Headache appeared first and was paroxysmal and generalized, attacks lasting an hour or two; described as being "bursting" in nature. During this illness patient

had several short attacks of weakness affecting left arm and leg. These symptoms lasted acutely for three weeks and then passed off, but patient continued to suffer from paroxysmal headaches. In August, 1929, the acute symptoms recurred with great severity. Headache and vomiting lasted for one month. Left arm and leg became weak and sensation was impaired on left side for short periods of 30 minutes at a time. Similar transient attacks of loss of speech recurred frequently. Left-sided weakness diminished and was succeeded by weakness and impairment of sensation in right arm and leg. During this month the patient suffered for a fortnight from diplopia but there was no history of observed strabismus. Since the acute illness in August she has suffered frequently from paroxysmal headaches.

She has suffered at intervals since the age of 14 from acute attacks similar to those described above, being perfectly well in the intervals. These previous attacks were of varying severity lasting from one to three weeks. They were all associated with short attacks of left hemiparesis and aphasia. They occurred at intervals of several years, but have become more frequent during the last seven years. During the latter period most of the attacks have been associated, when they were at their height, with loss of consciousness lasting, e.g., for 24 hours.

During all the acute attacks vivid visual hallucinations have been present, chiefly when the patient was in the dark or when her eyes were closed. A carpet would unroll itself towards her and smother her, or someone was standing beside her, etc. Vertigo was marked during all attacks.

Since April, 1929, mistiness of vision has been present in the left eye.

Physical Examination.—Cranial nerves: pupils moderate in size, equal and regular. Pupillary reactions normal. Extra-ocular movements normal. (On September 3, 1929, there was difficulty in conjugate deviation to the left.) Vision: mistiness in left eye. Left $\frac{6}{6}$, right $\frac{6}{5}$. Discs: in August, 1929, there were three dioptres of papillœdema in the right eye with hæmorrhage into the disc. This papillœdema has diminished. Disc reddened to the colour of retina and edges blurred; left disc pale. Fields: left, normal; right, markedly contracted, particularly in inferior nasal quadrant. Corneal reflexes, present and equal. No facial paresis. Hearing and speech normal. Other cranial nerves normal. Sensory system normal. Motor system: trunk muscles normal. Power slightly diminished in right arm. Power seems slightly impaired in both legs. Tone, range of movement and coördination normal. Reflexes: abdominal absent. Tendon reflexes present, equal and not exaggerated. (A few months ago knee- and ankle-jerks were exaggerated on the left side.) Plantars flexor. No Rombergism. No sphincter incontinence. Gait: a little uncertain. The patient is left-handed.

Commentary.—Cerebrospinal fluid normal and not under increased pressure. Wassermann reaction negative in cerebrospinal fluid and in blood. Skiagram of skull normal. Ventriculography and other tests for hydrocephalus not performed.

Clearly the patient has been suffering from a rise in intracranial tension. She has suffered from a precisely similar condition at intervals for many years. When first seen the diagnosis of cerebral tumour was naturally entertained. However, none of the signs and symptoms suggests definite localization of a lesion. A tumour could probably not produce recurrent attacks of raised intracranial tension, with perfect health in between, over so long a period. The diagnosis that best seems to meet the facts is that of recurrent attacks of acute internal hydrocephalus.

The long history, absence of progression, and of focal signs, render the presence of a slow-growing tumour as the cause of the hydrocephalus doubtful.

A diagnosis that suggests itself is that of a chronic remittent form of meningitis serosa—a condition which may closely simulate a cerebral tumour. The cause of this condition has been ascribed to a chronic ependymitis—either causing serous effusion into the ventricles or obstructing the iter or medullary foramina. Hypertrophy of the choroid plexuses is another cause.

Arachnoiditis following Acute Mastoiditis, and leading to Obesity.—W. RUSSELL BRAIN, M.D.

History of Illness.—A schoolboy, aged 12, had pain in the right ear on July 27, 1929, with temperature of 102° F., and vomited twice two days later. August 3, 1929, admitted to London Hospital under care of Mr. W. Morris.

Previous History.—Treated at Radium Institute for nævus of left cheek.

Condition on Admission.—Drowsy. Complained of headache. Temperature 103° F. Signs of acute otitis media. Paracentesis of drum carried out next day. On following day ear began to discharge and temperature fell. August 6, 1929, temperature was normal but his pulse fell to 48 and tenderness was found over right mastoid process, bilateral papillœdema and nystagmus. Mr. Morris performed an incomplete mastoidectomy and exposed a perisinal abscess which he drained. Drowsiness, bradycardia and papillœdema persisted. August 19, 1929, optic discs showed + 4D of swelling, diplopia had developed, with weakness of left external rectus. August 20, 1929, Mr. Morris operated again. Right lobe of cerebellum explored with sinus forceps, but no abscess found. August 26, 1929, papillœdema amounted to + 4D right, and + 5D left.

August 30, 1929, he showed, in addition to the papillœdema, weakness of left external rectus, nystagmus on conjugate deviation in all directions, and a slight weakness of right lower face. In the limbs there was general hypotonia, but no weakness, ataxia or adiadokokinesis. Tendon reflexes sluggish, abdominal reflexes present, plantar reflexes flexor. No sensory loss. Visual fields full. No cervical rigidity; Kernig's sign absent.

On August 31, 1929, papillœdema was right + 2·5D, and left + 3·5D. Lumbar puncture performed. Cerebrospinal fluid pressure was 460 mm. of fluid and manometer showed exaggeration of arterial and respiratory movements. Ten c.c. of fluid were withdrawn. This contained three very degenerate white cells, "probably lymphocytes," per c.mm.; protein 0·01 per cent.; Wassermann reaction negative.

On September 4, 1929, papillœdema had diminished to + 2D in both eyes, and there was no weakness of the left external rectus. Cerebrospinal fluid pressure was now 115 mm. of fluid. Slight swelling of the discs remained until November 16, and they now show secondary optic atrophy. Visual acuity: right $\frac{6}{9}$; left $\frac{6}{12}$.

Obesity developed during convalescence; patient gained 19 lb. in two months. Skiagrams of head show no abnormality. Sugar tolerance test: fasting blood-sugar 0·105 per cent.; 50 grm. of glucose given; three-quarters of an hour later blood-sugar 0·133 per cent.; two hours later 0·118 per cent.

There is possibly slight genital atrophy.

? Lead Myositis.—E. A. CARMICHAEL, M.D.

A. M., aged 57. *History.*—As under-gardener by trade, enjoyed good health until April, 1929, when abdominal pain developed. In May, pain became more severe and was accompanied by retching: towards end of May he noticed that his hands were "closing up" and becoming weak. No contact with lead could be discovered.

Family and Past History.—Nothing relevant.

On Examination.—Pale; gums unhealthy and have a blue line along margin; this blue line is not punctate. Aortic second sound accentuated. Blood-pressure: 216 systolic; 105 diastolic. No abnormality detected in urine.

Nervous System.—No cranial nerve lesion; bilateral drop wrist; extensors of wrist very weak; flexors fairly strong. Supinatores longi working well. Some atrophy of weakened muscles. No sensory disturbance; reflexes normal. Trunk and legs show no abnormality.

Blood-count.—Red cells 3,990,000, hæmoglobin 75%, white cells 5,200.

Basophil stipling present. Wassermann reaction negative. Examination of urine negative for lead.

Fits of Major Epileptic Type associated with Progressive Bilateral Facial Paresis and Bulbar Symptoms.—HUGH G. GARLAND, M.R.C.P.

F. H., a boy, aged 12, admitted to National Hospital, Queen Square, under Dr. Critchley, on November 13, 1929, complaining of fits, difficulty in eating and drinking, with constant dribling of saliva and slowness of speech, all of four years' duration.

Family History.—Father died from war wounds, mother alive and well. No fits, insanity, or paralysis on either side. One sister, two step-brothers and two step-sisters alive and well. Mother had no other pregnancies.

Previous History.—Full-time child. Difficult labour with instrumental delivery. Pertussis when aged one year, measles when aged two years. Appeared quite normal up to age of five, when adenoids and tonsils were removed. Then began to have a winter cough, frequent feverish colds and bronchitis. Varicella at age of six years. Vaccinated in infancy. Pneumonia in December, 1928. Has always been thin.

History of Present Illness.—At age of eight years began to have attacks whilst in bed at night, would sit up in bed, draw himself into an attitude of general flexion and then turn his head, eyes and tongue to the right, with limbs slightly flexed. After maintaining this attitude for about three minutes his limbs would suddenly relax and he remained exhausted for a short time. He was incontinent in these attacks and used to bite his tongue and become blue, but always told his mother afterwards that he could hear whatever was said by onlookers during the whole attack.

When these attacks first began he had about two each night, within twelve months; the intervals between the fits slowly decreased to about a quarter of an hour but still the fits occurred only at night. About twelve months after the first fit he began to have fits in the daytime as well.

The daytime attacks began with trembling of both sides of upper and lower lips. There was no cry, and at first he paused but did not fall down, but within a few months these attacks became worse so that they seemed to throw him down with lower limbs flexed, right more than left, and stiff; complete recovery occurred after a minute except for some tremulousness. The attacks during the daytime increased gradually in frequency until he was having one every fifteen minutes in the daytime as well as at night. These attacks occurred until Easter, 1928, when the day attacks ceased suddenly. The night attacks continued, but have lessened, in frequency in the last few months and had been less severe in the week before admission. The character of these attacks also changed recently so that instead of sitting up he stretched out stiffly and his arms and legs would go into clonic spasm after an initial tonic contraction. Incontinence occurred less often with the improvement in attacks and lately has not occurred at all.

Coincident with the onset of attacks in the daytime (i.e. three years ago), the boy began to dribble and have difficulty in eating and drinking. He held his mouth open habitually, and fluids began to run out of the corners when he attempted to drink. He often choked over his food, with regurgitation of fluid through nose and mouth. His speech, previously good, became very slow and laboured.

When the day attacks ceased, early in 1928, the difficulty in eating and drinking, and dribbling of saliva diminished a great deal, but the speech did not improve. About six weeks before admission these symptoms reappeared in exaggerated form.

Occasional pains shooting from the right side of the nose upwards and outwards over the right supra-orbital margin, have occurred during the last three years. No change in frequency or severity of attacks during this time. The pain usually lasted about a day, but a week before admission he had an attack which lasted three days, and was followed by epistaxis with relief of pain.

Morning headaches about once a month since onset of fits, but no vomiting.

Occasional spitefulness with other children during the last three years, but otherwise no change in behaviour. Vision unimpaired. Has never seen double. No cough since last winter.

On Examination.—A boy of average development for his age, with smooth, expressionless face, and slow, stiff, facial movements when these occur. Face pale and puffy; skin of forehead and nose smooth and shiny. Coöperates well on examination, slow in comprehension, but intelligence fair. Voice monotonous, speech exceedingly slow and syllabic; frequent omission of syllables and occasional nasal intonation. Labials noticeably slurred. No twitching or tremor in any part.

Cranial Nerves.— No anosmia. No abnormality detected in visual acuity, fields or fundi. Both pupils slightly irregularly circular; reaction to light, though brisk in both, is not well held, with ensuing hippus. Ocular movements jerky; a few irregular rapid jerks occur on extreme deviation to either side. No strabismus or diplopia, slight bilateral ptosis. Corneal reflexes brisk and equal.

Poor amplitude in all facial movement; right side moves better than left on voluntary movement, and vice versa on emotional expression.

Palatal reflex is sluggish but present; palate moves in midline in voluntary movement. Cannot whistle. Mr. T. H. Just reported that, on laryngeal examination, "the cords were pearly white and moved normally."

Tongue deviates to left on protrusion, is protruded well and without tremor; left side slightly less bulky than right; edge more bevelled, and feels thinner on palpation, but no fibrillation.

Motor power good for all movements in both upper limbs. Fingers gradually flex a little when limbs are outstretched, but no tremor or athetotic movements. Marked hypotonia in both upper limbs but coördination tests well carried out. Both upper limbs thin and there is slightly less bulk in the interossei of the left hand than of the right. No fibrillation detected.

Motor power good for muscles of neck, trunk and lower limbs. Cannot cough. Both lower limbs hypotonic except for extensors of left hip, which appear slightly spastic. Left foot held slightly inverted. No atrophy or fibrillation in lower limbs.

Tendon jerks exaggerated, with ill-sustained ankle clonus on left side. Abdominal reflexes more easily fatigued on left side. Plantar responses flexor on right, and equivocal on left. Occasionally undoubted extensor response. No loss of sensation could be detected.

Nothing abnormal detected in chest or abdomen. Teeth all showed deficiency in enamel over crowns.

Gait: Flat-footed and left leg not lifted well, but no ataxia or spasticity. Arms swing well. No Rombergism on standing.

Report on cerebrospinal fluid, November 19, 1929: Pressure 110 mm., clear, colourless, no cells seen, total protein 0·025%, Nonne-Apelt and Pandy negative, Lange no change in any tube. Wassermann reaction negative in cerebrospinal fluid and also in blood.

Lateral and antero-posterior skiagrams of skull revealed no abnormality.

During period of admission to hospital patient has had a number of fits, all except one occurring in sleep. Onset is sudden, with pallor, jerky movements, turning of head to right, absent corneal reflexes and incontinence of urine. Duration about three minutes, with no after-effects other than drowsiness and further sleep. He has had as many as three attacks in one night but usually has only one.

One attack occurred while awake. In this he felt a sudden twitching sensation in the right upper lip, followed by turning of the head upward and to the left and rigidity with twitching in all limbs, beginning on the right side and extending to the left. The duration was about one and a half minutes and in the latter part of the attack the corneal reflexes were lost and the patient became cyanosed. There were no after-effects.

Hysterical Gait with Organic Signs.—EMANUEL MILLER, M.D., and W. OGILVY REID, M.B.

N. C., a girl, aged 12, was observed one year ago to be walking peculiarly. Inability to use left hand properly noticed about same time. Both disabilities have increased gradually since. Nothing of interest in past history.

Family History.—Father suicide. Otherwise clear.

Present Condition.—Cranial nerves: slight weakness of left lower face otherwise normal. Tone and deep reflexes increased in left upper limb. Latter retarded in development—arm, forearm and hand being smaller than on right side (about 1 in. of total shortening).

Fine tremor of both hands. Abdominal reflexes present and equal. Tone and deep reflexes increased in left lower limb. Plantar reflex flexor. Slight weakness of extensor muscles of left foot. No tremor. There is half an inch shortening of left leg. Left side of face is smaller than right. Nævus in right fronto-temporal region. No sensory changes; sphincters normal.

Gait.—Sways to left as if tending to fall in that direction, and suggests that of a slight left hemiplegia.

Psychological Background.—Intelligence normal. States she had a "big fright" when she heard that her father had been killed by falling from a beam. (Considerable abreaction when talking of this.) Attachment of child to father appears to have been very great, and gait is apparently a mimetic reaction to father's death, which took place under tragic circumstances just before onset of patient's present condition.

Spondylose Rhizomelique.—REDVERS N. IRONSIDE, M.B.

W. C., male, aged 22. Nine months ago had a febrile illness, and was in bed for ten days. On second day after getting up, weakness of neck muscles was noticed and he was unable to hold his head up. Lately has had difficulty in rising from sitting position. Eight weeks ago these symptoms became rather worse.

On Examination. — Optic discs, pupils, and cranial nerves are normal. Limitation of movement in cervicodorsal spine at both shoulders and at both hip-joints with wasting of pelvic and shoulder girdle muscles. No sensory loss; all tendon reflexes brisk and equal, plantars flexor. Pectoral muscles, superficial cervical muscles and superficial muscles of back give normal electrical responses. No evidence of bony changes shown by skiagrams. Cerebrospinal fluid normal. Wassermann reaction negative in blood and cerebrospinal fluid.

Specimens from Three Cases of Primary Malignant Disease of the Pancreas.—W. E. CARNEGIE DICKSON, M.D., and W. REYNELL, M.D.

I.—Large Secondary Growth in Left Cerebral Hemisphere, for which a Decompression operation was performed. Shown at a previous Meeting of the Section, and now shown again for comparison with the second Specimen.—*History:* D. C., male, aged 35, an accountant, was admitted to the West End Hospital for Nervous Diseases, November 15, 1927, complaining of weakness and loss of weight, dating from the previous February. In June, 1927, a left-sided pleurisy developed, with pain, fever, dyspnœa and hæmoptysis. In September, 1927, he suddenly lost the use of the right arm and leg, and had severe headache, but no loss of consciousness; three days later he lost his voice. The headache continued, and vision became impaired, with (as noted on admission) papillo-œdema (right 3, left $3\frac{1}{2}$). The left pupil was larger than the right, and there was nystagmus both to right and left. There was loss of power in the right arm and spasticity of the left leg, the reflexes being more marked on the right side, with right extensor plantar response. The right abdominal reflex could not be elicited.

A left lateral decompression was performed December 7, 1927, and a gradually

increasing hernia cerebri supervened, with mental confusion and deterioration, and extreme loss of weight and strength. Death occurred on January 21, 1928.

Post-mortem (January 21, 1928).—A large primary adeno-carcinoma of the pancreas, with extensive secondary growths in the upper retroperitoneal glands and mediastinal glands, with invasion of heart and both lungs (with bronchiectasis and pneumonia of left lung), and an enormous metastasis in the centrum ovale of the left cerebral hemisphere. In all these situations the histological structure of the secondary growths was identical with that of the more rapidly-growing parts of the primary pancreatic tumour.

II.—Large Secondary Growth in Brain similar to that in (I) and in similar position, with Necrosis, Softening, and formation of Pseudocyst, into which some Hæmorrhage has occurred.—*History :* H. C., male, aged 44, a clerk, who had been working until about six weeks before his death, though he "had not been feeling well" before that. He was taken ill while at work and sent home, and what was described as a "stroke" came on. He was confined to bed and became very weak, and only semi-conscious, but had no "fits." Admitted to hospital, November 27, 1929, in a condition of semi-stupor, mentally deranged, and with a left-sided hemiplegia and left-sided facial paresis. The right optic disc was blurred, the left clear. He gradually became worse, developed double incontinence and terminal hypostatic pneumonia, and died December 8, 1929.

Five days before death the cerebrospinal fluid was clear and colourless, showing only five cells—all "small lymphocytes"—per c.mm., total protein 0·05%, with a trace of globulin, a colloidal gold curve of 0112110000, and, as also in the blood, a negative Wassermann reaction.

Post-mortem (December 9, 1929).—Extensive malignant disease affecting the pancreas (primary), both suprarenals and kidneys, upper abdominal lymph-glands, etc. (but not the liver), and mediastinal glands. A mass the size of a small orange in the right lower lobe of the lung, and a small nodule in the heart-wall.

The brain showed marked flattening of the convolutions, with "baggy" softening of the right cerebral hemisphere towards its anterior half, found to be due to a large pseudocyst formed by the necrotic softening of a large secondary mass of tumour, of which the walls were composed, the contents consisting of straw-coloured and slightly blood-stained fluid, probably partly derived from the lateral ventricle.

Histologically, the tumour in the head and body of the pancreas was found to be a primary carcinoma arising from the parenchyma of the gland, the secondary metastases (including the wall of the pseudocyst in the brain) showed a similar structure.

III.—Moderate degree of Hydrocephalus for which No Obvious Cause was discovered. There were widespread secondary growths involving kidneys, suprarenals, omentum and mesentery, abdominal and thoracic glands, heart and lungs, but not brain.—*History :* H. C., male, aged 58, admitted to hospital, June 12, 1929, complaining of winter-cough for the past six years, and an attack of "influenza" about five months before admission, with subsequent fits of depression and lack of power of concentration. A right empyema was diagnosed, and the fluid from an exploratory puncture contained numerous large cells, single and in clumps of three or four up to several dozen, and a provisional pathological diagnosis of tumour made. The Wassermann reaction was negative in the blood, and a polymorphonuclear leucocytosis of 25,600 per c.mm. was present (June 25, 1929). No tubercle bacilli were found in the sputum, in which also no tumour-cells were identified on repeated examination. In November, 1929, some small subcutaneous nodules of tumour were noticed, one of which was excised for microscopical examination. Some parts of this were suggestive of a "cancer,"

though the appearances in other parts might be interpreted as those of a mesoblastic pulp-tumour.

A rib was resected August 3, 1929, and a cavity (found, post-mortem, to be breaking-down tumour) drained. Death occurred on August 18, 1929.

Post-mortem.—A medium-sized firm nodule of new growth was found in the head of the pancreas, and an enormous mass of matted new growth firmly bound together the spleen, tail of the pancreas, left suprarenal and kidney, and lymphatic glands, etc. Numerous nodules and masses were also present in the omentum, mesentery and liver. Very large masses were also present in the mediastinum, with invasion of the pericardium and base of the heart, and both lungs, especially the right, and pleuræ. In the head, there was a small nodule in the centre of the floor of the left middle fossa, between the dura and the bone, but not infiltrating the brain, which appeared to be atrophied, with exaggeration of the sulci and excess of cerebrospinal fluid.

The lateral, third and fourth ventricles, and also the aqueduct of Sylvius, all showed moderate but distinct dilatation, for which no obvious cause other than atrophy of the brain (?) could be detected.

Histological sections of the tumour in the head of the pancreas showed it to be a rapidly growing adeno-carcinoma, with all stages of chronic interstitial pancreatitis in the surviving portions of the gland.

In the fat of the omentum and in the fat round the kidneys, etc., typical areas of "fat-necrosis" were present, as might also be seen in the naked-eye specimens.

The various secondary nodules in the organs and tissues (including a minute nodule in the posterior lobe of the pituitary body near its junction with the anterior lobe) all showed a structure analogous to that of the more actively growing parts of the primary pancreatic adeno-carcinoma.

Sections of the choroid plexuses did not show anything of note, beyond some slight fibrosis between the vessels and surface cells, of which there was no active proliferation.

Specimen: Large Gliomatous Tumour in Right Temporo-sphenoidal Region and spreading extensively in Right Hemisphere.—W. E. CARNEGIE DICKSON, M.D., and C. WORSTER-DROUGHT, M.D.—A spongioblastoma multiforme supervening upon an old, partially encapsulated gumma. *History:* A. M., male, aged 51, diagnosed two years previous to admission as a case of general paralysis. Admitted to hospital June 28, 1929, with history of obsessional neurosis. Had a "fit" six months previously and was drowsy, and had gradual loss of power in left arm and leg for two weeks.

He died two days after admission, from hypostatic pneumonia of both lungs.

Post-mortem, a large soft gliomatous tumour was found, with a central yellowish area microscopically shown to be an old gumma. At the lowest part of the mass, gumma only was found.

Section of Psychiatry.

[*January* 14, 1930.]

The Pathology of the Senile Psychoses.

By MACDONALD CRITCHLEY, M.D.

THE modern histological conception of the senile psychoses dates from the work of Alzheimer, who, in 1892, first drew a clear distinction between the brain changes due to cerebrovascular disease and those due to senility. In this way, arteriosclerotic dementia was clearly separated on a pathological basis from the group of senile dementias.

Although we are no doubt on perfectly safe ground in thus sharply distinguishing arteriosclerotic dementia from senile dementia, it must be remembered that this distinction is more of theoretical than of practical importance. It is true that senile dementia may exist in pure form clinically, and be unaccompanied by any demonstrable disease of the cerebral blood-vessels. Such cases, however, must be rare, and in the majority of instances the cerebral arteries share in the senile changes present in the brain. How far the clinical features and the pathological anatomy are altered by these associated changes we do not know, and the problem is one which has been entirely unexplored.

Probably the best manner of approaching the question of the pathology of the senile psychoses is to consider first the anatomical changes in the brain occurring in healthy old age. In this way we obtain our starting-point by becoming conversant with the type of tissue upon which pathological changes become implanted. Moreover, one avoids the error of labelling as pathological certain peculiarities which are normally present in the senile brain. The term "healthy old age" is one, of course, which is at once a challenge. It is a matter of opinion how far one is justified in speaking of a normal senium, and some would agree with Cicero in regarding old age itself as a disease. Everyone who has devoted attention to the subject will admit the very great difficulty in setting a dividing-line between the states of senescence and of senility, whether the criteria be psychical, physical or anatomical. Until the solution of this question is within sight, it will be advisable to use as a working hypothesis Rolleston's definition of old age as a "physiological or normal process of involution, with progressive atrophy and loss of vitality and free from any morbid change due to other factors, extrinsic or intrinsic."

The Senile Brain.—The pathological brain changes in the normal senium can be considered briefly. On naked-eye inspection a certain amount of atrophy is visible, causing widening of the sulci. There may be a reduction in weight amounting in exceptional cases to 200 grm. Trans-section reveals some ventricular distension; thickening of the meninges may be encountered. Sclerosis of the basal arteries is frequently present, although not an essential feature.

Histological changes in the senile brain may be discussed under three headings: neuronal changes, neuroglial alterations, and depositions of amorphous material.

Neuronal changes comprise first a disappearance of a number of nerve cells from the cortex. This process is most marked in the frontal and prefrontal regions. There is, however, a similar numerical atrophy in the cells of the basal ganglia and

locus niger. Von Braunmühl has drawn attention to an especially severe affection of the cells of the olives in old age. Various pathological changes may at times be present amongst those cells which remain; they include:—

(*a*) Fatty degeneration of the cells.—This change, in Stief's opinion, constitutes the most constant and characteristic feature (fig. 1).

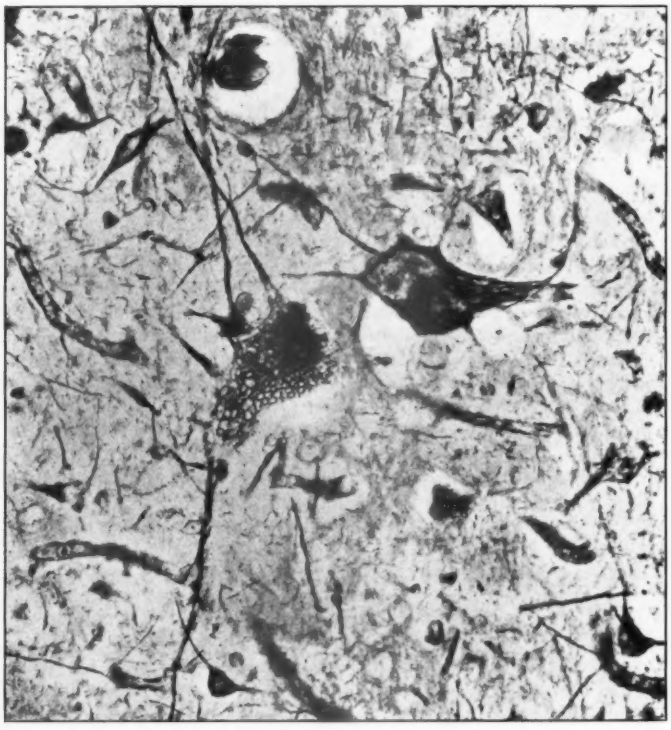


FIG. 1.—Motor cortex from the brain of a "normal" old woman aged 103. Two Betz cells are seen, one of which shows an advanced stage of fatty degeneration. (Bielschowsky stain.)

(*b*) The intracellular fibrillary tangles of Alzheimer (fig. 2).—These may be described in Alzheimer's own words:—

"... in the interior of the cell which is otherwise normal, one or more fibrils are conspicuous on account of their special thickness and the density of their impregnation. Later, other neighbouring fibrils participate, and these form thick bundles lying in the periphery of the cell. Finally, the cell with its nucleus disappears, and the site becomes marked by a spiral-like bundle of fibrils."

All stages of this process may be demonstrated, ranging from simple intensification of the intracellular fibrillary network to a mere cellular "skeleton" made up of tangled, densely-staining coils (figs 3 and 4). Certain histologists, such as Bielschowsky, Simchowicz and others, believed that these structures are of neuroglial formation and lie outside the cell; the majority, however, regard them as neurofibrillary innature.

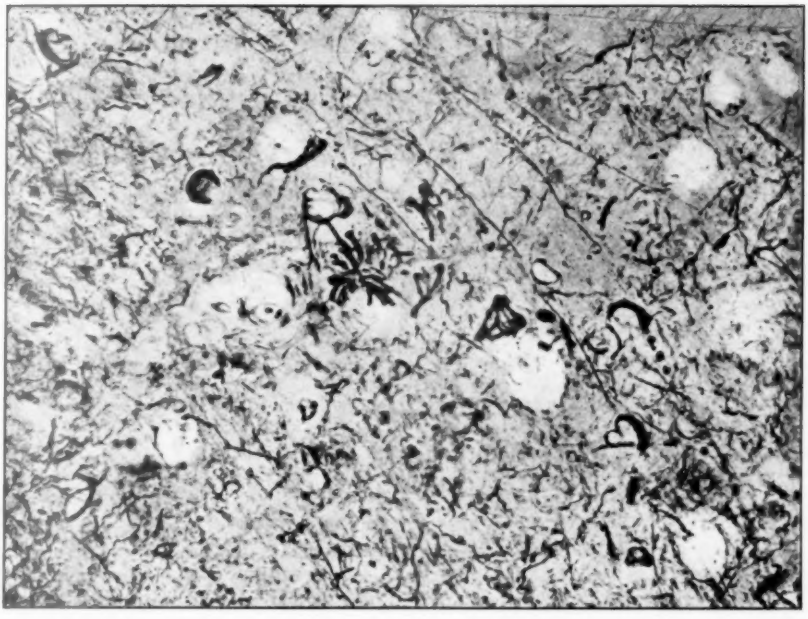


FIG. 2.—Cerebral cortex of same patient showing several nerve cells with Alzheimer's intracellular neurofibrillary alteration. In the centre is an early senile plaque. (Bielschowsky stain.)

FIG. 3.—An advanced stage of Alzheimer's intracellular fibrillary alteration. (From Ley : "L'anatomie pathologique de la sénilité," *Journ. de Neur. et de Psych.*, 1923.)

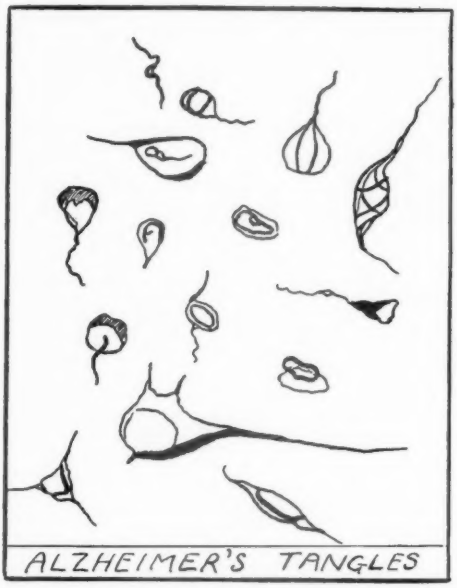


FIG. 4.—Sketch illustrating various types of Alzheimer's "tangles" or intracellular fibrillary alteration.

(*c*) Bouman has drawn attention to a peculiar alteration in the Purkinje cells occurring in advanced age, especially in the presence of mental change. The typical appearance comprises a spindle-shaped swelling of the proximal portion of the axons; the interior of the swelling is homogeneous, but a netlike structure may be observed in the periphery. Vacuolation may occur at a later stage. Bouman describes the Purkinje cells with their axonal swelling as "torpedoes."

Disappearance of the neurone leads to a relative demyelinization which may be demonstrated in certain areas by the use of Weigert-Pal staining methods. The tangential fibres in particular show this change.

Glial changes of both a regressive and a proliferative character are commonly encountered. The latter usually take the form of a diffuse gliosis of the brain, more intense in certain regions. Thus, subpial, subependymal and perivascular types of gliosis are usually demonstrable, with the frequent appearance of "monster-cells." In these situations a reticulated appearance often occurs. The regressive changes in the glia include the finding of rod cells (Stäbchenzellen), especially in the molecular layers of the cornu ammonis. Grynfeltt's mucocytic degeneration of the oligodendroglia may also be demonstrable. Microglia cells may be somewhat more numerous, and there is usually an increase in the amount of protoplasm.

In the senile cerebellum, the neuroglial changes differ in being essentially patchy. The gliosis is limited to the perivascular zones, the depths of the fissures, the white matter surrounding the dentate nuclei and the regions immediately around the Purkinje cells. Rod cells may be visible in the white matter.

The combination of diffuse cerebral gliosis with neuronal atrophy leads to shrinkage and loss of weight of the whole brain. There results an internal and external hydrocephalus *ex vacuo*. The shrinkage may be most marked in the regions of the loci perforatus posticus and lateralis where the brain substance falls away

from the basal arteries, causing wide dilatation of the perivascular spaces. On cross section of the brain, this is revealed by the appearance of numerous lacunes of disintegration, particularly in the region of the basal ganglia and internal capsule.

FIG. 5. – Subependymal and perivascular glial proliferation in the brain of a "normal" old man aged 101. (Stained with Greenfield's modification of Mallory's phospho-tungstic acid stain.)

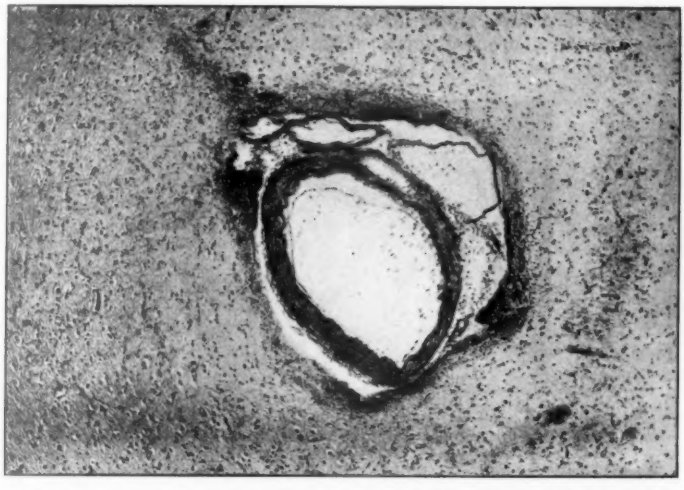


FIG. 6.—Perivascular gliosis in a normal old man aged 101. (Greenfield-Mallory stain.)

Certain authors have described under the term "klasmatodendrosis," fragmentation of the prolongations of the neuroglia into the white matter, as a feature of the senile brain. Bonfiglio, however, believes this to be a post-mortem change.

FIG. 7.—Gliosis surrounding lacunes of disintegration in the region of the posterior perforated spot, in a normal old woman aged 103. (Greenfield-Mallory stain.)

Amongst the various types of deposition within the senile brain may be mentioned:—

(*a*) *Corpora amylacea*, especially in the fimbria (fig 8). These bodies may be collected together in groups, especially around the blood-vessels, but they are always separated by minute neuroglial fibres. Oseki has described this appearance under the term "état gruyère."

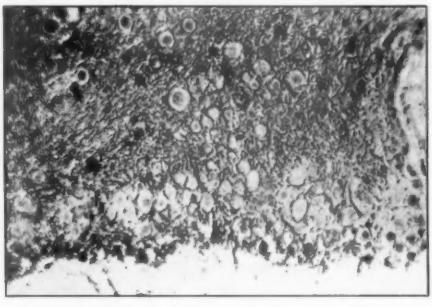


FIG. 8.—Corpora amylacea in the fimbria of a senile dement, *Riv. di patol. nerv. ment.*, 1924, 29, 295. (Mann's stain; magnification 210 diameters.) (From Rizzo.)

(*b*) *Senile plaques* in the cortical grey matter (fig. 9). These are small, circular areas of densification scattered throughout the cerebral cortex, staining intensely with silver impregnation methods. The plaques vary considerably in individual appearance, but certain form-constants recur, viz., rings, radial figures, star-shaped structures and circular homogeneous areas (fig. 10). Frequently, a nuclear-like body of amorphous or cellular nature may occur in the centre. Histo-chemical examination of the plaques

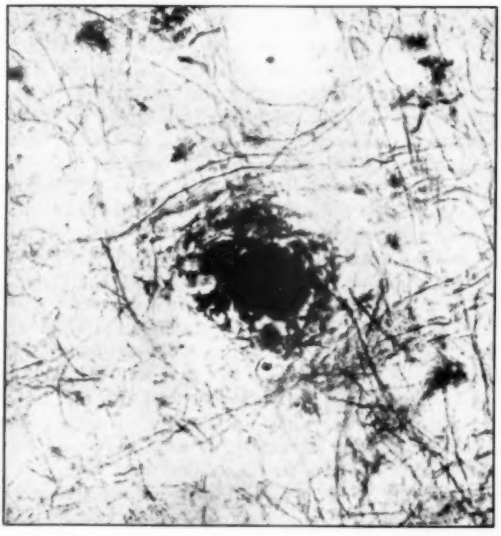


FIG. 9.—A senile plaque shown under high magnification; from the cerebral cortex of a case of senile dementia in a man aged 91. (Levaditi stain.)

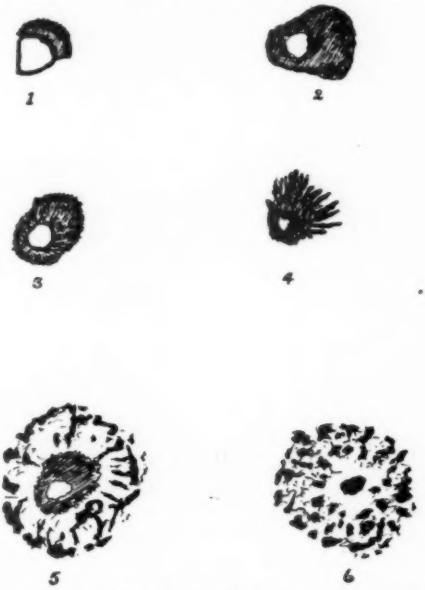


FIG. 10.—Schematic representation (after Bouman) of the genesis of a perivascular type of senile plaque. (1) Densification along one aspect of the blood-vessel. (2) The densification extends around the vessel, but is still more marked on one side ("signet-ring"). (3) The most distal portion of the dense area became hazy. (4) Exaggeration of the same process. (5) The radial process extends outwards to end in a ring-like structure at the periphery ("the wheel" or "morning-star"). (6) The blood-vessel itself atrophies. (From Critchley: "Nature and Significance of Senile Plaques," *Journ. Neur. and Psychopath.*, 1929. Reproduced by kind permission of the Editor.)

reveals the presence of some substance allied to amyloid in the centre; lipoid may also be demonstrable within the plaque. Microglia plays an important rôle in the formation of these bodies, although neuroglia and oligodendroglia do not participate. Neurofibrils and, at times, myelinated axis cylinders may be seen. The nature and genesis of the senile plaques have been the centre of widespread and prolonged controversy. To-day they are usually regarded as a special type of tissue-reaction directed against a specific and toxic metabolic process. A primary involutional alteration in the chemistry of the fundamental ground-substance of the nervous system is believed to cause depositions of lipoid or possibly amyloid material. These precipitates are strongly argentophil in staining reaction. A microglial reaction is provoked; Hortega cells become incorporated and insinuate themselves into the innermost portions, where they themselves undergo degeneration. In this way are built up the bodies which we know as senile plaques.

(*c*) The "*fatty plaques*" of Laignel-Lavastine and Tinel are possibly entities distinct from the ordinary senile plaque, although Rizzo regards them as artefacts.

There is a lack of certain knowledge as to the extent and relative frequency of the various histological changes in the senile brain. Diffuse fatty degeneration and a moderate degree of numerical atrophy in the nerve cells and glial proliferation constitute the common findings. Alzheimer's tangles may be entirely absent in an individual specimen. Thus no such alteration was found in the brain of one centenarian I have examined, although a widespread though not intense diffusion of Alzheimer's tangles occurred in the cortex of another patient aged 103. I doubt whether senile plaques often occur in the absence of psychical change during life; they were absent from the brains of two patients aged 101 and 103 respectively, which I have studied. Costantini found only a very few plaques in the brain of his "normal old man of 105." Huebner, Simchovicz, Léri and many others, however, describe them in small number in the brains of the aged, increasing in number with advancing years.

The Senile Dementias.—The pathological anatomy of senile dementia in the majority of cases is characterized by an exaggeration of the various histological processes noted in the case of the senile brain. Most pathologists insist that the objective cerebral changes differ from those in the normal senium only in degree; in other words there is no absolute anatomical criterion of senile dementia, and no abrupt frontier between the territories of pathology and physiology.

Examination of a large series of specimens indicates that in dementia the intensification of the pathological changes of senility is not necessarily an evenly distributed process, but may exhibit a selective tendency. Thus, in the so-called presbyophrenic variety of dementia, it was believed that an unusually marked development of senile plaques was characteristic. We now believe that the clinical basis of some of these cases called presbyophrenia was uncertain, and that the brains rich in plaques typically represent the pathology of *dementia senilis simplex*.

Although senile plaques may possibly occur in the absence of dementia, their presence in large number throughout the cortex is strongly suggestive of dementia. Should the patient be not particularly advanced in years, this evidence is strengthened. In typical instances the plaques will occur in the greatest number in the frontal and temporal regions, and may even be demonstrable in fewer numbers in the central grey matter, the pons and mid-brain, the cerebellum and spinal cord.

The usual pathological picture of dementia senilis simplex therefore comprises an exaggeration of the microscopical changes of senility with a preponderating development of senile plaques.

Whether it is possible to correlate more closely the various clinical subtypes of dementia with a distinct pathological picture, is not yet known. Thus we cannot at present recognize the brain of a depressed senile dement as being different from that of an agitated or confused patient.

Consideration of the pathology of some of the atypical and "presenile" varieties of dementia reveals that the changes may here also show different varieties of selective development.

Pick's disease, for example, illustrates the purest variety of specialized anatomical change. In this condition there is a marked neuronal atrophy limited to certain regions of the cortex. The other pathological changes of senile dementia, such as Alzheimer's type of fibrillary alteration, and plaques, do not occur. Glial changes of moderate degree exist, but are purely secondary phenomena.

Characteristically, there is a numerical atrophy of the cortical neurones, most obvious in the three upper cell laminæ; the nerve cells which remain may be swollen, but otherwise are not grossly altered in appearance. The diagnosis is revealed macroscopically by a marked convolutional atrophy with widening of the sulci (fig. 11). The atrophy may affect the whole of the cortex, but much more frequently is limited to certain regions; the frontal, temporal, and occipital lobes may be affected in this way. Both hemispheres are usually affected, often with striking symmetry.

There is no obvious explanation of the peculiar distribution of the pathological change in this malady; the atrophy does not correspond with vascular territories, and changes in the cerebral vessels are exceptional and non-essential. There is no correspondence with the zones of myelinization as plotted by Flechsig, but Gans has pointed out that in some cases there may be a striking parallelism with Brodmann's cytoarchitectonic areas.

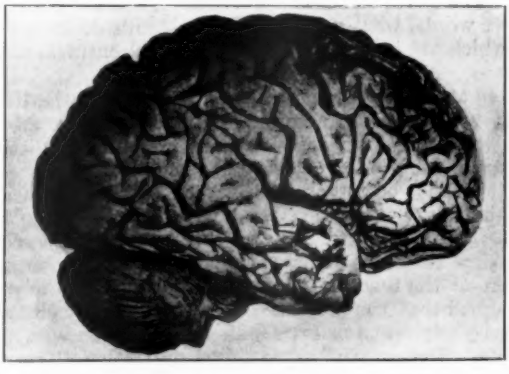


FIG. 11.—Extreme atrophy of the frontal regions of the brain in a senile psychotic probably representing a case of Pick's disease. (From Blackburn's "Gross Morbid Anatomy of the Brain in the Insane," Washington, U.S.A., 1908.)[1]

Pick's disease may, therefore, be regarded from the standpoint of pathology as a type of involutional process in which cell atrophy is the all-important feature.

In that type of presenile psychosis known as Alzheimer-Perusini's disease, we find in addition to the histopathological changes of senility a preponderance of intracellular fibrillary change. Nerve cell atrophy, neuroglial proliferation and plaque-formation may also occur in some measure, but do not constitute the outstanding feature.

Alzheimer's disease may therefore be looked upon as a type of premature involutional change within the brain, in which the preponderating tissue reaction comprises the development of alterations in the intracellular fibrils.

[1] With acknowlegments to the Government Printing Office, Washington, U.S.A.

The pathology of presbyophrenia has not yet been determined with any degree of certainty. At the beginning of this century there was a definite tendency to associate the presence of senile plaques with the diagnosis of this disease. Fischer was the chief exponent of this view; but within more recent years, Uyematsu has pointed out that Fischer's idea of presbyophrenia hardly corresponded with Wernicke's original description, and that Fischer's cases will fall into the cadre of senile dementia, as defined by the American Psychological Association. The more recent studies suggest a close similarity between presbyophrenia and Alzheimer's disease, as regards the pathological picture.

Claude and Lhermitte have drawn attention to another histological variety of senile psychosis which they describe as "Diffuse atrophic cortical sclerosis." This condition presents no obvious clinical points of differentiation from dementia senilis simplex but is distinguished on anatomical grounds by a preponderating overgrowth of the neuroglial fibrils, especially in the cortex.

Claude and Lhermitte's psychosis may therefore be regarded as a subtype of senile dementia in which neuroglial proliferation is the outstanding pathological feature.

It appears, then, that in the varieties of senile psychoses certain of the histological criteria of senility may be exaggerated so as to dominate the picture. Thus, we may have a neuronal atrophy as the outstanding feature—as in Pick's disease; or an excessive fibrillary alteration—as in Alzheimer's psychosis; or an intense plaque formation—as in dementia senilis simplex. One is probably justified in pushing this argument still further and hypothesizing the existence of other varieties of senile psychosis—as yet unidentified—with distinct clinical and pathological pictures. In other words, what we to-day term "senile dementia" may be actually a pigeon-hole in which are concealed many nosological entities, which are allied and yet discrete.

Stief has hinted at the same hypothesis when drawing attention to those cases of senile dementia which are characterized pathologically by an absence of senile plaques. He suggests that such cases actually represent a distinct and possibly diagnosable subtype of the general category of senile dementia.

A note of caution must be struck with regard to slavish attempts to associate clinical with pathological phenomena and with regard to the belief that histopathology can set the seal of finality to this neuro-psychiatric problem. The chemical and physical reactions of nerve-tissue to various dyes are, at the best, a very rough measure of the functional integrity of that tissue during life. It must not be lightly assumed that the presence of scarred or degenerated structures in a brain has necessarily any direct or even indirect connection with signs or symptoms observed during life. These pathological débris are rather the outward signs of a particular type of tissue-reaction to a factor which, while perhaps incapable of ocular demonstration, must nevertheless be regarded as the original basis of both clinical and pathological anomalies. Thus, the presence of numerous senile plaques throughout the cortex of a senile patient does not reveal the immediate cause of the anterograde amnesia, or the intellectual enfeeblement noted during life. The plaques are rather themselves the evidence of a special reaction in the tissues to a metabolic anomaly. Simchovicz has affirmed that the brain of a relatively young senile dement is histologically indistinguishable from that of a normal old man of 100. But although the pathology of the two conditions may be identical, the clinical and psychiatric pictures are probably widely dissimilar.

We are probably nearer the truth if we regard the pathological findings in the senile psychoses as the marks of the reaction of a senile tissue to some outside agency. As the nature of the agent varies, so the histological reaction alters, giving the reaction of a cell atrophy in one case, a neuro-fibrillary reaction in another, and plaque formation in a third.

Evidence in favour of this conception is demonstrable in the fact that the common histological findings in the senile psychoses may also be met with in conditions far removed from senility. Thus, swelling of the Purkinje cells (Bouman) has also been seen in some cases of disseminated sclerosis (Doinikow), in cerebellar atrophies (Sträussler; Rossi), in juvenile G.P.I., in amaurotic family idiocy (Sträussler), and in schizophrenia (Schroeder). Senile plaques have also been observed in a few cases of Korsakow's psychosis (Simchovicz; Marinesco), and in tabes (Tiffany). Alzheimer's tangles resemble strikingly the phenomena observed by Cajal after section of the central axon (Achúcarro and Gayarre), while the various types of regressive change in the glia are found in diverse conditions.

Another question of extreme interest is raised by those cases in which certain anatomical and physiological units within the brain are the exclusive seat of senile processes. There is some evidence to suggest that portions of the nervous system may at times be endowed with a limited viability, so that they are doomed to decay earlier than the rest of the nervous system. Gower's abiotrophic maladies—such as Friedreich's ataxia—may exemplify this point. Of more immediate interest are those maladies occurring in the last third of life, characterized pathologically by a local neuronal decay.

Idiopathic Parkinson's disease is the best instance of a senile process limited to the palæo-striatum. According to the views of Jelgersma, Lewy, Jakob and others, we are here dealing with a localized process of senility. We may indeed associate ourselves with Stief in regarding the motor anomalies of paralysis agitans as an exaggeration of the alterations in gait, stance, posture and movement characteristic of old age.

Under the title of "senile rigidity" Jakob has drawn attention to a not uncommon combination of mental change and movement-disorder occurring in extreme old age. In Jakob's disease—as it may well be called—a patient far advanced in years gradually deteriorates mentally until the psychical state of senile dementia is attained. A little later, a definite Parkinsonian syndrome develops so that finally the picture of paralysis agitans becomes superimposed upon a dementia. The pathology of this condition is characterized by the formation of plaques and other senile lesions in the corpus striatum and in the cortex.

A limitation of senile histopathological alterations to the cortex of the cerebellum is found in the rare disorder known as delayed cortical cerebellar atrophy. In this condition the signs of a progressive cerebellar dysfunction are linked with an atrophy of the palæo-cerebellum (Edinger). Exceptionally, as in the case reported by van Bogaert and Bertrand, mental enfeeblement—presumably due to cortical implication—may co-exist. Senile atrophy of the neo-cerebellum is exemplified in the syndromes described as olivo-ponto-cerebellar atrophy and olivo-rubro-cerebellar atrophy.

Conclusion.—There exists to-day an urgent need for fuller detailed information with regard to cases of senile dementia, fuller clinical data together with accurate psychical and neurological analyses, minute histological examinations with the employment of the newer techniques of the Madrid school, and more judicial correlation of the clinical and anatomical aspects, with particular attention to the anomalous and exceptional cases which seem to belong to no particular category.

Section of Surgery.

[*December* 4, 1929.]

Specimens from a Series of Cases of Gastro-jejunal Ulcer.—CECIL A. JOLL, M.S.

I.—W. A., male, aged 41.

Posterior gastro-jejunostomy and appendicectomy March 24, 1927 (C. A. J.). At operation a duodenal ulcer was found in the first part of the duodenum, adherent to the pancreas. Twenty-two years' history of typical attacks of pain two hours after taking food, and waking him at night. Fractional test meal showed a typical climbing curve. He remained free from symptoms for six months, after which the symptoms recurred.

Second operation January, 1928, when a large penetrating ulcer was found on the jejunal aspect of the anastomosis, involving the stoma in its anterior aspect. Operation consisted of excision of loop of jejunum, end-to-end anastomosis followed by excision of distal two-thirds of stomach and Polya's anastomosis.

II.—G. C., male, aged 45. Posterior gastro-jejunostomy and appendicectomy (November, 1925) (C. A. J.). At operation an ulcer was found on the antero-superior aspect of the first part of the duodenum and the appendix was fibrotic and bound down by adhesions, the lumen being obliterated. Seven years' history of typical attacks of pain and vomiting and loss of 1½ st. in weight. Fractional test meal showed a curve within normal limits and no delay in emptying of the stomach. When seen again in October, 1926, he was putting on weight, and, apart from occasional flatulence, was quite free from symptoms and was carrying out the usual instructions with regard to diet. He returned in December, 1926, complaining of recurrence of symptoms, which continued, in spite of treatment, for twelve months. The pain was now in the umbilical region, and was at its worst two hours after food; he had lost one stone in weight.

He was re-admitted to hospital in December, 1927, and it is interesting to note that he was then suffering from gingivitis. At operation a gastro-jejunal ulcer was found. The affected loop of jejunum was excised and gastrectomy was carried out by the usual technique. The specimen shows that the ulceration was confined to the gastric side of the anastomosis.

III.—L. W., male, aged 49. Anterior gastro-jejunostomy and appendicectomy (June, 1926) (C. A. J.). The usual posterior operation could not be performed owing to the short transverse meso-colon. At operation an ulcer half an inch in diameter was found on the posterior-inferior aspect of the first part of the duodenum, and there were many adhesions between the duodenum and the gall-bladder. Five years' typical history previous to operation. Fractional test meal showed a typical climbing curve. When seen again in January, 1927, he was losing weight; there had been no improvement at all since the operation, the pain was, if anything, worse, and he was vomiting practically every day. X-ray examination at this time showed that the stoma was not working well and the barium tended to adopt a circular route through the pylorus. The radiologist reported that there was probably a jejunal ulcer near the stoma inside the distal lobe of the jejunum. Fractional test meal showed an acid curve slightly above normal, bile present in all specimens and no delay in emptying of stomach.

Re-admitted February 7, 1927, when a blood examination was made, with the following findings: Red cells 4,040,000, hæmoglobin 75%, colour-index 1.

One thousand c.c. of 10% glucose saline, with 20 units of insulin, were administered intravenously on February 9, 1927, and an operation was performed on the following day. The old duodenal ulcer was found to be unhealed, and there was a large jejunal ulcer present in the efferent loop, ¾ in. from the stoma. Resection of the loop of jejunum involved in the anastomosis was carried out with end-to-end anastomosis, followed by resection of the distal two-thirds of the stomach, the end of the duodenum being buried and a fresh loop of jejunum joined to the stomach by Polya's method.

IV.—W. A., male, aged 35. Duodenal ulcer. Posterior gastro-jejunostomy, 1913 (Sir Harold Stiles). Remained quite well until 1916, when recurrence of symptoms was noticed, the pain being chiefly on the left side. In 1919 operated upon at Gravesend Civil Hospital for perforation of a jejunal ulcer from which he made a successful recovery, but has suffered since that time from repeated attacks of pain and one attack of hæmatemesis three years ago.

Operation, December, 1926 (C. A. J.): A small jejunal ulcer was found close to the stoma, and excision of the affected portions of the jejunum with end-to-end anastomosis, followed by resection of the distal two-thirds of the stomach, was carried out.

The specimen showed a small jejunal ulcer close to, but not involving, the stoma on the anterior aspect.

V.—S. T., male, aged 30.

Operation for an appendix abscess in Leicester Royal Infirmary, February, 1925. Posterior gastro-jejunostomy, August, 1926. Ulcer found on upper and posterior aspect of first portion of duodenum. Three and a half years' history of typical attacks of pain. Quite free from symptoms until February, 1927, when, following an accident causing severe concussion, the symptoms recurred. The pain was now above and to the left of the umbilicus; it came on immediately after the taking of food and was not relieved by medical treatment. Operation (C. A. J.), January, 1928, at which a small jejunal ulcer was found and excision of the affected portion of the jejunum and gastrectomy were carried out,

The specimen shows the portions removed at the second operation turned inside out, and a small jejunal ulcer can be seen ¼ in. away from the line of anastomosis. Embedded in the floor of the ulcer is a small portion of plating from an instrument, part of which has been removed for examination.

VI.—A. P., male, aged 24. Operation (C. A. J.), January, 1927. Posterior gastro-jejunostomy and appendicectomy. Small duodenal ulcer found on anterior aspect of first part of duodenum. Three years' history of typical attacks of pain. After operation was quite free from symptoms for four months, when recurrence occurred, and attacks continued at intervals. He had followed out the routine dietetic scheme, and he started smoking six months after operation.

X-ray examination in October, 1929, showed the duodenal ulcer still unhealed and a jejunal ulcer near the stoma. At a further operation in November, 1929, excision of the affected portion of the jejunum and partial gastrectomy were carried out.

Mr. MAX PAGE said that the incidence of gastro-jejunal ulceration was considerably higher than was suggested by most published figures. He had had the opportunity when at a Pensions Hospital of seeing a large number of gastric cases in which the patients had undergone gastro-enterostomy, and had found it necessary to operate on twenty-seven cases for symptoms of gastro-jejunal ulceration. In his experience, in quite a large number of such examples the gastro-jejunal ulcer was the only remaining lesion. If on a digital examination of the mucous membrane of the stomach no ulcer was felt, the proper procedure was to restore, as far as possible, the gastro-intestinal canal to its normal relationships. In his opinion, this operation, though often a tedious one, was associated with less risk to the patient than that of a partial gastrectomy.

Specimens shown by CECIL P. G. WAKELEY, F.R.C.S.

I.—Annular Pyloric Carcinoma.—The specimen shows an annular hard white carcinoma at the pylorus. Microscopically it is a spheroidal-celled carcinoma.

Clinical History.—Mrs. B. E. F., aged 49, admitted to hospital September 6, 1929, had been for eighteen months suffering from constant pain in the epigastrium. Vomiting had occurred at times, and the patient was getting considerably thinner. A small hard movable tumour was felt in the region of the pylorus. Partial gastrectomy was performed September 18, 1929. There were no enlarged glands, or any signs of secondary deposits. Patient was discharged October 9, 1929, in good condition.

II.—Fibroma of Jejunum causing Intussusception.—The specimen shows a loop of jejunum with a large tumour in its wall causing an intussusception. Microscopical examination proved the growth to be a fibroma.

Clinical History.—Mrs. R. C., aged 52, admitted to King's College Hospital on December 8, 1928, suffering from acute obstruction. Had complained of abdominal pain since August, 1928. The pain was intermittent at intervals varying from one to five minutes. Patient often felt sick but never actually vomited. The bowels were opened daily without purgatives.

At the end of September, 1928, the pain became much more marked, causing the patient to double herself up and cry out frequently. She began to have attacks of vomiting, usually twice a week, and a large amount of yellow material was brought up. There was no relief of pain, however. She could not take any solid food and she lost weight rapidly. Constipation commenced, and aperients had to be taken to produce an action of the bowels.

In November she was examined by X-rays, and chronic obstruction of the small intestine, due to adhesions in the region of the spleen, was reported.

She became weaker and the vomiting increased. Condition on admission: temperature 97·6, pulse 100, respiration 20. Anxious expression. Vomiting. Bowels open two days previously. Tongue furred and flabby. Double dentures. Marked abdominal distension with visible peristalsis round the umbilicus. Nothing abnormal found on palpation.

Laparotomy (December 8, 1928). Right paramedian incision. Large intussusception of the lower part of the jejunum was found. Partial reduction only was possible, as the gut was very friable and œdematous. Enterectomy was performed, 5 ft. of intestine being removed. The openings of the gut were stitched up, and a lateral anastomosis was performed.

The wound healed *per primam*, and convalescence was uneventful. Patient was discharged from hospital December 29, 1928.

III.—Cystic Kidney in an Infant.—The specimen shows a large cystic kidney which has been sectioned in a vertical axis. Numerous cysts are visible, varying in size and containing what appears to be gelatinous material.

Clinical History.—H. J. C., a male infant, aged one year and eight months, was admitted to Dr. Still's ward at King's College Hospital, April 6, 1929, with an abdominal tumour. When he was a year old his mother noticed a swelling on the right side of the abdomen, which gradually increased in size. It never seemed to cause any trouble or pain.

On examination.—The right side of the abdomen was occupied by a large smooth tumour of firm consistence, like solid rubber, extending up to the liver margin, just across the mid-line, and below into the iliac fossa.

Urine 1020. About four pus-cells and two blood-cells per field. No casts.

April 17, 1929.—Blood-urea 39 mgm. per 100 c.c.; April 19, blood-urea 38 mgm. per 100 c.c.

Operation April 22, 1929, under open ether. A right paramedian incision was made, extending from the costal margin to two inches below the umbilicus. The inner border of the rectus sheath was opened, the rectus muscle displaced outwards, and the posterior sheath carefully incised. The peritoneum was pushed inwards by gauze dissection. A large solid renal tumour was exposed. The peritoneum was incised, and the left kidney palpated. It appeared to be normal to the touch. The peritoneum was closed. The renal tumour was delivered into the wound.

There were many aberrant renal vessels; the pelvis of the kidney was greatly dilated.

The ureter was ligatured and divided with a carbolized knife. The kidney was then removed and the wound closed.

Recovery was uneventful. Discharged May 26, 1929. Has been seen every two months since the operation, and is perfectly well in every way.

Microscopical Report.—There is no normal kidney tissue present; the normal structure is completely replaced by a number of cysts varying in size from 0·1 mm. to 5 mm. in diameter, lying in a fibrous stroma.

The type of epithelium lining the cysts shows considerable variation. In some of the cysts the epithelium is definitely columnar, the cells having large vesicular nuclei situated towards their bases; in other cysts, including the smallest, the epithelium is very flattened, and the cells resemble endothelial cells. All intermediate types are represented. In all the cysts the epithelium is only a single cell thick. The loose fibrous stroma shows areas of hyaline degeneration. There has been hæmorrhage into the stroma mostly recent, but there is also some pigment present, chiefly within phagocytes. The stroma shows areas of infiltration with inflammatory cells, including large numbers of plasma cells.

IV.—Fibro-Sarcoma of the Jejunum.—The specimen shows a loop of proximal jejunum with a portion of the mesentery. In the concavity of the loop a hard tumour can be seen obstructing the lumen of the gut. There are some enlarged lymphatic glands to be seen in the mesentery. Microscopical examination of the tumour proved it to be a fibro-sarcoma.

Clinical History.—The specimen was removed from a man aged 57 years, who had suffered from indigestion for over a year previous to operation. When first seen, June, 1929, there was visible peristalsis, and a tumour could be palpated in the region of the umbilicus. No vomiting.

Laparotomy, under gas and oxygen anæsthesia, June 24, 1929. A hard tumour was discovered in the jejunum, eighteen inches from the duodeno-jejunal junction. A V-shaped enterectomy was performed, and an end-to-end union of the bowel established.

The patient recovered remarkably well and was allowed to get up on July 13, nineteen days after the operation; pneumonia developed later, however, and he died July 18, 1929, twenty-four days after the operation.

Unilocular Cyst of the Spleen.—C. MAX PAGE, D.S.O., M.S.

The cyst formed a tumour about the size of a boy's football. The wall appears to be composed of firm fibrous tissue except where it is made up from the compressed remains of the spleen; this area has the appearance of normal splenic tissue and it occupied the upper and outer sector of the mass. The cyst contained about three pints of a brown grumous fluid in which there was much cholesterol. Red cells and leucocytes were also present. Professor Dudgeon reports that, microscopically, the wall was of fibrous tissue showing evidence of hæmorrhages and acute inflammation. Portions of the wall were partly necrotic.

Clinical History.—The cyst was removed from an engine fireman, aged 26, who gave a history of having strained his left side when twisting a brake in the summer of 1926. He was subsequently confined to bed for eight weeks the condition being diagnosed as pleurisy. He then returned to work and remained fit

till April, 1928, when the pain in the left side and the dyspnœa recurred. He was off work for seventeen weeks. Treated by X-rays. He resumed light work for a short time but was not free from pain. Admitted to St. Thomas's Hospital under Dr. Cassidy on October 31, 1929.

On examination, a cystic swelling filling in the epigastric angle could be palpated. It extended 2 in. below the left costal margin. Thoracic organs normal. Wassermann and Sachs-Georgi reactions negative.

Skiagrams showed that the cardiac end of the œsophagus lay an inch to the right of the mid-line, and that the stomach was completely displaced into the right hypochondrium.

A blood-count showed hæmoglobin 107% and white cells 6,000 per c.mm.

Operation, November 6, 1929. Ether anæsthesia. Five-inch left paramedian incision beginning 1 in. below costal margin. On opening the peritoneum a smooth cystic surface mass presented. About 2 pints of fluid were drained off by puncture, and it was then found that the cyst was adherent to the end surface of the diaphragm on the left side, but was otherwise free. The adhesions were broken down and the cyst delivered on to the surface of the abdomen together with the flattened remains of the spleen which was integral with its wall. The pedicle of this was divided and ligatured in detail and a few bleeding points in the sub-diaphragmatic area were also tied off. The wound was resutured without drainage.

The patient made an uninterrupted recovery complaining only of some sensation of unusual mobility in the stomach. Got up November 19, and returned home November 24, 1929.

Discussion.—Unilocular splints of the spleen of the character described are rare. They have generally been regarded as blood or degeneration cysts. The subject has been discussed fully by Fowler,[1] who reports about sixty-five cases of large cysts collected from the literature up to 1921. Novak and Wallace Frank describe cases and state that they have found six other cases in the literature up to 1927.[2] The exact pathology of the condition seems to be obscure. The size and character of the tumour are hardly consistent with its being due to a simple hæmorrhage. In the case here described, microscopical evidence suggests the presence of some inflammatory reaction in addition. In the cases described in the literature, a history of trauma of some kind has nearly always been forthcoming. The age-incidence appears to have been between twenty and forty.

Cancer of the Small Intestine.—ZACHARY COPE, M.S.

A man, aged 60, gave only about two months' history of pain and vomiting. When examined there was a large mass felt in the left hypochondrium. Barium enema negative. No barium meal was given. Pre-operative diagnosis : cancer of the stomach.

At operation a large mass was found consisting of two coils of small intestine ; there was an obvious stricture and a mass in the mesentery thought at the time to be glandular.

Excision of both coils with mesentery. Closure of ends and lateral anastomosis. Uninterrupted recovery.

The specimen consists of the two coils with mesentery which contained an abscess owing to rupture of growth into mesentery. The growth was four inches from duodeno-jejunal junction.

Retrosternal Goitre removed after Resection of Inner Half of Clavicle.—ZACHARY COPE, M.S.

The patient was a man, aged 53, who had suffered from shortness of breath for fifteen years. He was excused from Army service during the late war on this account.

1 *Ann. Surg.*, 1921, lxxiv, 201.
2 *Surg., Gyn. and Obst.*, 1927, xlv, 586 ; *Ann. Surg.*, 1927, lxxxv, 360.

Recently breathlessness worse. Seen by physician who detected enlarged right lobe of thyroid. This did not appear to be sufficient to account for symptoms, so a skiagram was taken which showed large retrosternal goitre behind sternum and clavicle on left side.

Operation—intratracheal anæsthesia—rather difficult till inner half of left clavicle was resected. Then with two fingers placed in the superior mediastinum, by *vis à tergo* and *vis à fronte* the tumour, 5½ by 3½ in., was removed. A small tear in the pleura was sewn up. The tumour reached down to the aortic arch, which was seen pulsating at the bottom of the wound. Convalescence uneventful. The man's voice changed from tenor to bass in a night.

Paget's Disease of the Nipple.—Sir LENTHAL CHEATLE, K.C.B., F.R.C.S.

Since Sir James Paget first described this disease in 1874 a massive literature has accumulated upon the subject. The views of the various authors are most conflicting. It is to one of these views that I wish now to call attention.

Jacobaeus, Ribbert and recently Professor Robert Muir, of Glasgow, have ascribed the lesion of Paget's disease of the nipple to the spread of carcinoma cells, derived from a malignant tumour of the underlying breast, among the cells of the epidermis. The conception always seemed to me to be a mistaken one.

To assist in the determination of this matter I had bespoken the skilled services of Dr. R. J. Ludford should another case come under my care. It seemed that the only way to settle the matter would be to claim the services of an authoritative cytologist, and Dr. Ludford has kindly filled the rôle.

This is a picture of the state of things in this case seen macroscopically. [Drawing shown.] The case was that of a married woman, aged 70 years. Seven years ago she noticed the disease beginning on the top of her right nipple. It now occupies an extensive region covering the front and right side of the chest. In the centre of the lesion are many round, smooth, sensile protuberances about the size of the top of a thumb. Surrounding this area is the Paget's disease. Dr. Ludford will demonstrate that the cells in the area of the Paget's disease are purely epidermic in character and that the undulating prominences in the centre of the lesion consist of glandular carcinoma. Hence, in this case at all events, the Paget's disease is not due to a spread of breast carcinoma cells into the epidermis.

Dr. R. J. LUDFORD said: I have examined this case of Sir Lenthal Cheatle's as completely as possible from a cytological standpoint. The cytological examination proves that Paget's disease of the nipple is a purely epidermic condition, the cells of which could not have been derived from the mammary carcinoma cells of the underlying tumour.

During the course of the cytological examination the cells of the carcinoma in the breast and those of Paget's disease of the nipple have been investigated: (1) The chromophility of the cytoplasm (three methods). (2) The cell lipoids, including mitochondria (two methods). (3) The Golgi bodies. (4) The chromatin, as demonstrated by Feulgen's reaction for thymus-nucleic acid.

All stages of transition of epidermic cells were seen to be taking place in the same microscopic field from normal cells onwards. There are no malignant cells from the breast tumour in the epidermis in the area of Paget's disease.

Uterus with Fibromyoma, from which Hæmorrhage occurred into the Peritoneal Cavity.—J. P. ROSS, M.S.

The specimen shows a large fibromyoma projecting from the left cornu of the uterus and between the layers of the left broad ligament. Several enlarged and engorged veins are seen beneath the serous coat and one of them has ruptured.

Clinical History.—It was removed from a woman, aged 36, who had suffered for some months from occasional attacks of epigastric and suprapubic pain, associated with vomiting. Menstruation was regular, and there had not been menorrhagia.

The last regular period was fourteen days before admission to hospital, and after the period, pain in the abdomen, mostly in the epigastrium, had been more severe and

continuous. Twelve hours before admission there had been a sudden exacerbation of the pain, associated with faintness and followed by repeated vomiting.

On examination the patient was pale, sweating, cold and rather restless. Temperature 96°. Pulse 100 and poor volume. A freely mobile mass, about 4 in. in diameter, continuous with the cervix-uteri, was felt, and there were signs of free fluid in the abdomen.

A quantity of blood, estimated at a pint, was found in the peritoneal cavity, with clots in the pelvis and in the paravertebral fossæ. The source of bleeding was found to be one of the engorged veins over the fibroid. Hysterectomy was followed by rapid recovery.

Intraperitoneal hæmorrhage from a fibromyoma is a rare event, especially if unassociated with rupture of a degenerated fibromyoma, or torsion of the pedicle of a subserous tumour.

Specimens shown by L. R. BROSTER, M.Ch.

I.—**Hypernephroma.**—C. G., male, aged 53. Admitted to Charing Cross Hospital March 23, 1929.

Epigastric pain for three months. Pain in right hypochondrium for one month. Had lost three stones in twelve months. No urinary symptoms. There was a large hard, nodular tumour in the right loin, extending down into right iliac fossa and crossing the mid-line below umbilicus. Regular in outline, not movable. Nothing abnormal found in urine.

Operation, March 25, 1929. Laparotomy. A large retroperitoneal tumour was found growing from the lower pole of the right kidney. It was impossible to remove this growth, owing to hæmorrhage from the collateral circulation. Hæmorrhage arrested with gauze pack and wound closed. Swelling of left leg followed six days after operation. Became comatose. Blood-urea 155 mgm. per 100 c.c. Death occurred from uræmia.

Post-mortem examination showed the tumour to be a large hypernephroma extending into the renal vein. There was a small growth in the opposite kidney.

II.—**Secondary Hypernephroma in Femur, with Spontaneous Fracture after 9 Years.**—Mrs. E. T., aged 72. Admitted to Charing Cross Hospital under Mr. Clogg. Nine years previously right kidney had been removed by Sir John Thomson-Walker, who found a large hypernephroma in upper pole. Admitted to a cottage hospital with fracture of the upper third of the right femur. Three months later bone refractured.

On Admission.—Large pulsating swelling in the bone. Skiagram showed fracture due to endosteal tumour.

Amputation: Section of tumour showed typical hypernephroma. Blood-count showed slight reduction of number of red cells (4,280,000), and the presence of myeloblasts and myelocytes.

Summary.—(1) This case shows a late recurrence of hypernephroma in bone, the longest interval quoted being ten years. (2) The blood changes are diagnostic of secondary tumours in bone, often found before any radiographic evidence. These changes suggest that dissemination takes place, via the blood-stream and not lymphatics. Evidence is based on tumour cells in the blood-vessels, and in the absence of any infiltration of the lymphatic channels, especially those in the periosteum above the tumour.

Mr. MAX PAGE said that he had observed two cases in which secondary hypernephroma in bone was in evidence before the existence of the primary tumour had been recognized. In the last case, which he saw two years ago, the patient had a central growth in the tibia and a growth in the skin of the scalp, both of which were microscopically composed of hypernephroma elements. No evidence of kidney tumour could be recognized clinically or by X-rays.

Case of False Localizing Signs in Cerebral Tumour: Endothelioma of Left Sylvian Region revealed by Ventriculography.—L. R. BROSTER, M.Ch.

A. W., female, aged 26. Admitted to hospital April 15, 1929, on account of sudden failure of vision in both eyes.

Eighteen months' history of headaches varying in intensity; less severe during last three months; twelve months' history of vomiting, at first every day, recently once in three weeks; vomiting relieves headache.

Vision misty for a long time. Almost blind for last fortnight. Papillœdema both eyes. Absent corneal reflex *right* eye.

Loss of sensation over first and second divisions of fifth cranial nerve and neuralgic pain in this area, *on right side.*

Tumour probably under right temporal pole in close proximity to Gasserian ganglion.

Skiagram shows distortion of pituitary fossa.

Ventriculogram.—Right ventricle, fluid under pressure. Left ventricle, fluid scanty. Pain on injecting air. Air passed from right to left, but not from left to right.

Cerebrospinal fluid	Left	Right
Total protein ...	0·18% ...	0·020%
Globulin	heavy excess ...	no excess
Chlorides	0·700% ...	0·740%
Sugar	0·073% ...	0·068%

Specimens shown by H. C. L. WOOD, M.B., B.S. (for Mr. T. P. LEGG, C.M.G., M.S.).

I.—Sarcoma of Breast.—The specimen was removed at operation from a woman, aged 48. Lying within the breast is a mass of solid growth, in which there are numerous small hæmorrhages. There is noretraction of the nipple or of the skin.

Histological Structure.—The upper portion is an intracanalicular fibro-adenoma with an extremely cellular stroma. The ducts are occluded in some places by non-desquamating epithelial hyperplasia. One area has undergone hyaline degeneration. The solid growth is a fibrosarcoma, with spindle cells and a large number of giant cells.

Clinical History.—For two years patient had a swelling in the left breast: no symptoms. Large lobulated mass in upper and outer quadrant of left breast; soft and elastic; freely movable on deep structures; skin thinned and reddened slightly at upper and outer end (axillary) of tumour; ? slight dimpling of skin. Nipple normal: no palpable glands. Right breast normal. Healthy vigorous woman.

Operation.—February 25, 1928: Whole breast and pectoral fascia removed.

II.—Secondary Melanotic Deposits in Breast.—The specimen is a portion of the right breast of a woman, aged 38.

The section passes through the nipple. The substance of the breast is riddled with small foci of growth, some of which are deeply pigmented and others almost colourless. There is a large pigmented deposit lying within the subcutaneous tissues over the upper part of the breast. At the top of the specimen can be seen a lymphatic gland filled with pigmented growth.

Histological Structure.—Melanin containing carcinoma.

Clinical History.—In November, 1926, a pigmented mole was removed from underneath the right breast at the South London Hospital. Microscopically it proved innocent.

In February, 1927, a mass of deeply pigmented axillary glands was removed at St. Giles's Hospital.

On admission to King's College Hospital in July, 1927, the right breast was very much enlarged, and the skin over it was red, hot and œdematous.

Operation.—The breast was removed with a large area of skin and a few pigmented axillary glands. A large granulating wound was left.

III.—Sarcoma of Breast.—The specimen was removed from the left breast of a woman, aged 31, at operation. It is a large, apparently encapsuled growth, with a few small areas of hæmorrhage.

Histological Structure.—A spindle-celled sarcoma.

Clinical History.—The swelling was first noticed in June, 1926. On admission to hospital October 26, 1926, it occupied the whole of the upper half of the breast, was not attached to the skin and was freely movable. No enlarged glands were felt in the axilla, and a diagnosis of fibro-adenoma was made.

IV.—Branchial Cyst.—Patient, a woman aged 31. *History.*—January 2, 1924, a swelling appeared on the left side of the neck below the angle of the jaw. It varied in size, and was only painful when distended. It was tapped every fortnight until July, 1924, and a milky fluid drawn off (one quarter pint).

October 2, 1924, attempt at removal of cyst by family doctor.

Swelling reappeared soon afterwards.

December, 1924, another attempt at removal was unsuccessful. Swelling had been tapped occasionally, but gradually increased in size.

On Admission.—Lax, ill-defined swelling on left side of neck. Palpable from floor of mouth. *Extent*: Above to angle of jaw; below to thyroid cartilage; forward to middle of horizontal ramus; backwards to posterior border of sterno-mastoid and beneath it.

Fluid tested with starch solution and digestion took place. (Iodine indicator.)

Operation, October 23, 1929.—Cyst explored and found to be connected to pharyngeal wall by a pedicle. No connection with submaxillary gland.

Mr. E. W. RICHES said he wondered if the fluid aspirated from the cyst had been examined microscopically. The section shown contained crystals, some of which had the notched form of cholesterin. The cyst was lined by squamous epithelium, and it would be interesting to know the nature of the epithelium in the fibrous cord connecting it to the pharynx.

V.—Colloid Carcinoma of Breast.—Patient, a woman aged 73.

History.—Swelling, the size of a marble, noticed in left breast three years before admission, and discovered accidentally while washing. No pain at first. On January 2, 1929, a blood-stained discharge from nipple was noticed and the swelling became painful and tender.

On Admission.—The left nipple was replaced by a red, lobulated swelling about 1 in. in diameter. The skin was not ulcerated. In the breast substance there was a hard nodular mass, situated in the outer half of the breast and continuous with the superficial swelling. There was no attachment to the pectoral muscles. No enlarged glands could be felt, in either axilla or supraclavicular regions. The right breast was normal.

Operation (September 25, 1929).—Radical removal, including sternal portion of pectoralis major, pectoralis minor and axillary glands.

Histological Structure.—Colloid carcinoma.

VI.—Carcinoma of Ascending Colon.—Patient, a man aged 67.

History.—Admitted to hospital with a history of anæmia and extreme exhaustion of two and a half months' duration.

On Admission.—Skin slightly yellow. A hard nodular swelling could be felt in the right lumbar region, moving with respiration.

Barium enema: This showed a filling defect in the right ascending colon.

Fæces contained occult blood.

Blood-count.—Red cells 3,400,000; hæmoglobin 28%; white cells 10,200; colour-index 0·41.

Operation (October 24, 1929).—Resection of last 3 in. of ileum, cæcum and ascending colon and first 6 in. of transverse colon.

Lateral anastomosis between ileum and transverse colon.

Acute dilatation of the stomach developed forty-eight hours afterwards and the patient died October 30, 1929, the sixth day from the operation.

The specimen shows an annular carcinoma of the ascending colon.

Specimen: Lymphadenoid Goitre.—CECIL A. JOLL, M.S.

Removed from a woman, aged 53, by Mr. Ernest Miles, in May, 1914. The patient had complained of slight pressure effects. After the operation cachexia strumipriva developed. The patient has taken thyroid tablets regularly since then, and is in good health (November, 1929).

The drawing (fig. 1) shows the pale uniformly enlarged gland which retains no trace of the colloid-bearing tissue of a normal gland and which gives no indication that the pathological process has spread to surrounding tissues. There is some increase in the vascularity of the gland, indicated in the original by the conspicuously pink colour of the interlobular connective tissue shown. Microscopically (figs. 2 and 3) the change in the gland is absolutely uniform and consists essentially of a lymphoid infiltration of the connective tissue, each follicle being surrounded by lymphocytic cells. Colloid is conspicuously absent from the follicles.

This condition, which has been regarded as merely a stage in the development of Riedel's disease, differs from the latter in several important features both clinical and pathological.

(1) Lymphadenoid goitre involves the whole gland simultaneously. Riedel's disease is usually focal in origin though it may eventually affect the greater part of the gland; traces of normal thyroid tissue are almost always to be found.

(2) Lymphadenoid goitre never spreads to the infrahyoid muscles or to any extra thyroid structures even when the disease is watched for years. Riedel's disease quickly spreads to the extra-thyroid tissues.

(3) Lymphadenoid goitre rarely produces serious pressure symptoms. Riedel's disease often causes death from suffocation.

(4) Lymphadenoid goitre is rarely seen in patients under the age of 40. Riedel's disease is commonest in young adults and may be found in children.

(5) Lymphadenoid goitre is usually associated with hypothyroid symptoms even in its early stages. If a portion be removed to avoid pressure-symptoms, myxœdema often follows. In Riedel's disease even extensive operation is rarely followed by cachexia strumipriva.

(6) Lymphadenoid goitre does not show the dense fibrosis of Riedel's disease. The microscopic sections shown from two different specimens, one of long standing, reveal nothing comparable to the adult fibrous tissue seen in even early cases of Riedel's disease.

Figures 4 and 5 illustrate Riedel's disease. Both specimens were obtained from patients under the age of 30. Both show some colloid containing tissue remaining. In both there is evidence of involvement of surrounding structures. The microscopic section (fig. 6) illustrates the dense fibrosis spreading both inside and outside the gland. Severe pressure-symptoms existed in both cases. Operation in neither case resulted in any hypothyroid sequelæ.

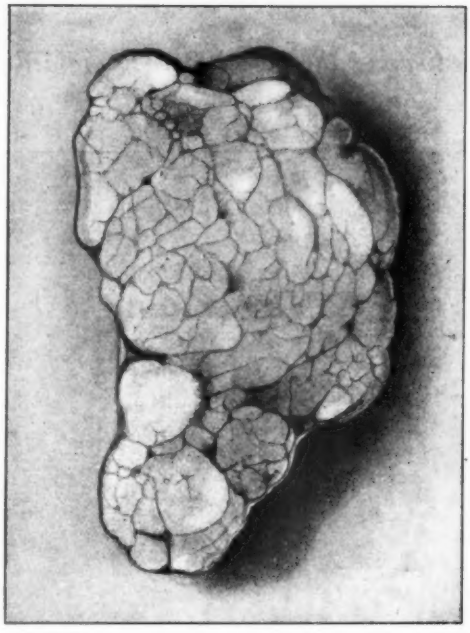


FIG. 1.—Lymphadenoid goitre. Pale and uniform structure. Interlobular connective tissue increased. No extension outside thyroid capsule.

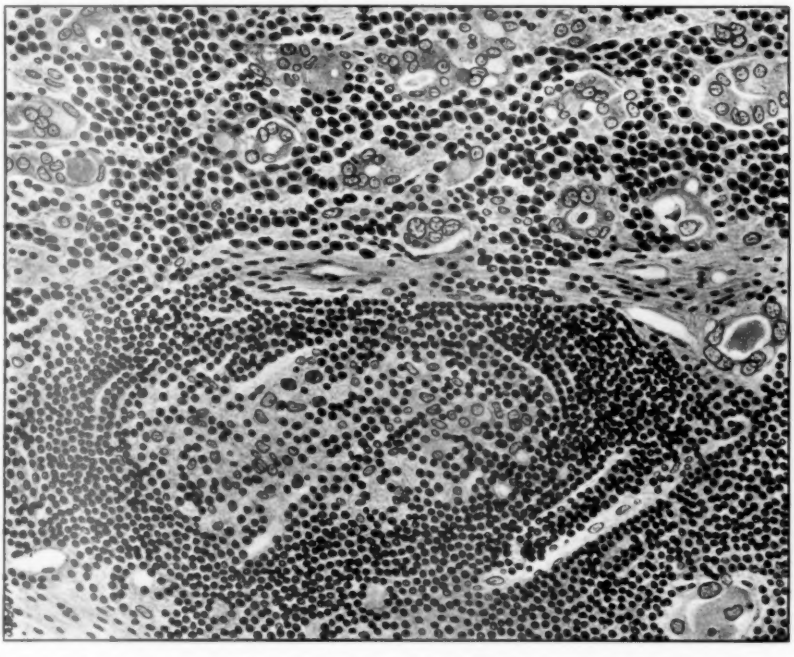


FIG. 2.—Lymphadenoid goitre ; section showing small vesicles, mostly colloid-free, lymphoid cells pervading the whole gland. One lymphoid follicle in centre. × 300.

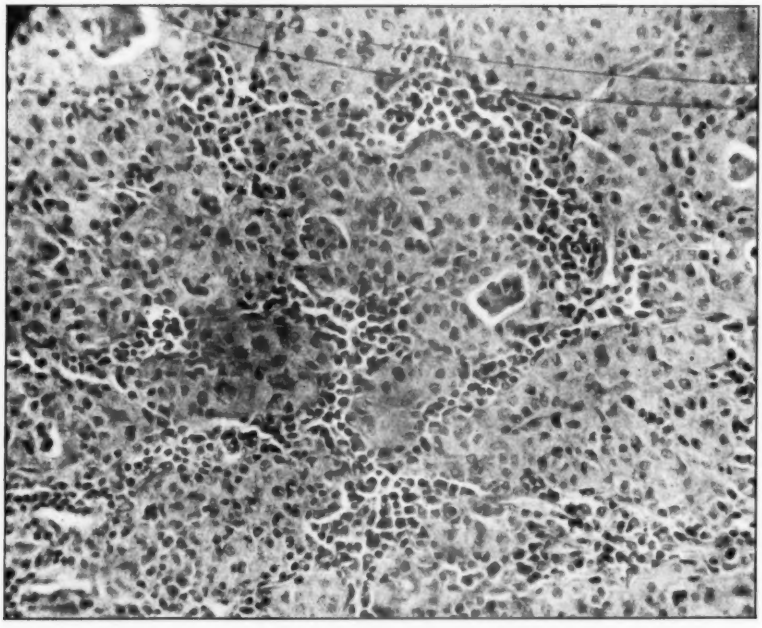


FIG. 3.—Lymphadenoid goitre; section showing the widespread lymphoid infiltration but no fibrosis. × 180.

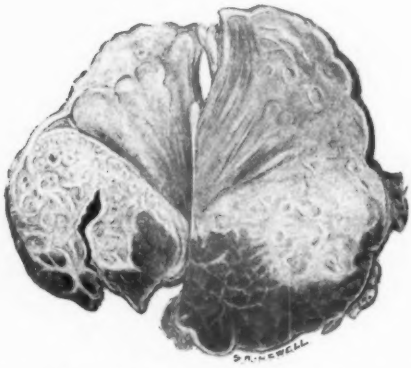


FIG. 4.—Riedel's disease: specimen showing dense fibrosis of the greater part of the gland, but a portion of healthy gland remains. Fragments of adherent muscle tissue can be seen.

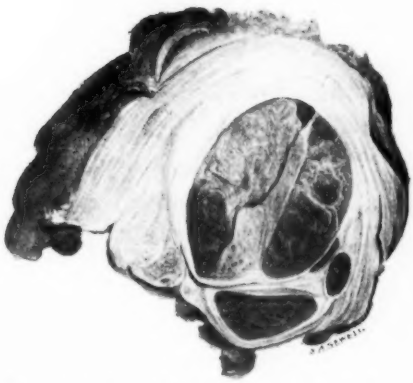


FIG. 5.—Riedel's disease; specimen showing in this case that the sclerotic fibrous tissue is chiefly peripheral, the surrounding tissues are involved but there is a central mass of recognizable thyroid tissue.

FIG. 6.—Riedel's disease: showing dense fibrosis; no trace of follicles remains. × 50.

JOINT DISCUSSION No. 2.

Section of Epidemiology and State Medicine and Section of Tropical Diseases and Parasitology.

[*November* 22, 1929.]

DISCUSSION ON BRUCELLA INFECTIONS IN MAN AND ANIMALS.

Captain W. Dalrymple-Champneys: I propose to consider first, the reasons why Brucella infections must be regarded as of great importance, not only abroad but also in this country; and second, the more important problems presented in this field.

The Importance of Brucella Infections.—The name "Brucella" was suggested by Meyer and Shaw for the genus comprising the *Micrococcus melitensis* and the *Bacillus abortus* (Bang's bacillus) in compliment to Sir David Bruce, who discovered the former organism in 1886 and shortly afterwards proved it to be the cause of Mediterranean (or Malta) fever; *Bacillus* (or *Brucella*) *abortus* is the cause of contagious abortion in cattle. It may seem unnecessary to insist upon the growing importance of human and animal infections with the organisms of the Brucella group, but from evidence which I have recently collected, I am convinced that not only are the general public unaware of the serious position in many European countries, but also a large proportion of the medical profession, in spite of the attention recently devoted to this subject in leading medical journals, still regard undulant (or Malta) fever as a tropical or subtropical disease of historical rather than practical interest. How far the veterinary profession is aware of the menace to human health from the organism causing that familiar disease of cattle, contagious abortion, it is not for me to say.

For these reasons, then, I shall review the facts which compel one to regard Brucella infections in man and animals as deserving the serious attention of the hygienist, the medical or veterinary practitioner and the statesman.

Undulant (or Malta) fever, which was regarded thirty years ago as a subtropical disease almost entirely confined to the Mediterranean littoral and islands, has now been recognized in every continent except Australia, and under climatic conditions ranging from those of Alaska to those of equatorial Africa. Moreover, the disease, or its recognition, is still steadily extending. I believe that in every country in which a serious effort has been made to detect the disease, its recognition has promptly followed. Recent striking instances are Denmark, Sweden, Holland, Switzerland, Canada, and Germany.

In Denmark the presence of Brucella infection in man was unknown until systematic investigations, by means of the agglutination test, were made yet 500 cases were discovered in the first twenty-three months, and more are continually being found. Kristensen tells me that the figures for January 1 to September 30, 1928, were 313 cases, and for the corresponding period of this year 395 cases. In the United States, where the search began earlier, at least 350 cases of undulant fever (according to Hardy) had been reported up to August, 1928. Wainwright collected official statistics showing 422 cases from January 1, 1927, to July 1, 1928,

and this does not give a fair estimate of the occurrence of the disease, for in certain States the disease was not made notifiable until July, 1928. In France, too, human cases of Brucella infection are known to be very numerous, the *melitensis* variety being apparently nearly always concerned. In the United States, Denmark, and Sweden, undulant fever appears to be a good deal commoner than enteric fever.

In view of such discoveries in neighbouring countries, can we afford to continue in ignorance of our true position in this country?

What is known of the disease in England and Wales? An exhaustive examination of the literature which I recently carried out for the Ministry of Health revealed records of only fourteen cases in which the disease is supposed to have been contracted in this country. While my report was in the press one other case was published, but during the last year or so I have received information with regard to a number of other cases, several of which I have seen but which have not been recorded, and I have no doubt that other unpublished cases are known. It has, then, been established that cases, apparently of endemic origin, do occur in this country, though only systematic investigations can give us any idea of their number.

In Malta, the Royal Society's Commission on Mediterranean fever showed in their classical investigations, that the goat was the cause of all the trouble; this animal is still responsible in some Mediterranean countries, the southern part of the United States and elsewhere, but in many countries its rôle has now been stolen by the cow. Strenuous efforts have been made to exculpate the cow, but in the opinion of most observers her guilt is now firmly established.

Besides the goat and the cow, several other animals, including the dog, pig, cat and sheep, have been shown to be capable of conveying the infection to man, the pig (in the United States) and the sheep (in France) being probably important sources of such infection.

I hope that this meeting will make it quite clear that undulant fever, though not a very killing disease, is responsible, in countries where it is prevalent, for a great deal of ill-health and suffering; that it often makes life a misery for its victims for months or even years; and that to describe it, as was recently done in a daily paper, as "not a very serious disease" is grossly misleading.

Problems presented by Brucella Infections in Man and Animals.

(I) *Transmission from Animals to Man.*—Transmission by means of goat's milk has been generally accepted as a fact since Dr. Zammit's classical demonstration in 1905, the *melitensis* variety of the organism being of course concerned, but the proposition that the milk of cows infected with Bang's bacillus (*Br. abortus*) plays a similar rôle, did not meet with the same ready acceptance. I believe, however, that any unprejudiced observer who carefully examines the evidence now available on this point will be convinced of the reality of such a mode of transmission, but this does not mean that all the problems connected with this phenomenon have been elucidated. We must still ask ourselves in every case in which the cow appears to be implicated: "Has this infection been transmitted by drinking the infected milk, or by direct contact with the cow or with matter contaminated by its secretions or discharges, or has an infection originally derived from cattle, been transmitted direct from man to man?" Kristensen, who has very thoroughly investigated the Danish cases, is now inclined to believe that though the infection in these cases was probably of bovine origin, yet in the majority—probably about 60%—some mode of transmission other than the consumption of infected milk, is indicated. Kling, on the other hand, tells me that he regards milk as the most probable source of infection in the Swedish cases. There are many cases in which the source and mode of infection are extremely difficult to determine, even when every facility for investigation is available. It is interesting to learn that in Denmark there is now a considerable

demand by doctors for milk for infants from farms free from contagious abortion, but such farms are often hard to find. In the United States, though the milk of infected cows is alleged to be the source of infection in most reports, yet pigs, both alive and dead, are being regarded with increasing suspicion. I have been unable to obtain any evidence of Brucella infection of swine in this country, but can we be certain that it does not exist? When I started my investigations I was told that the goats in this country were never infected with Brucella, but I have been able to show that this is not true, though what may be the extent of such infection I cannot say.

(II) *The Elimination of Danger from Cattle.*—This problem is perhaps the most important and difficult of all. Though a reverent follower of that great genius Pasteur, I cannot regard the mere destruction of Brucella in infected milk as an adequate defence against this danger, even if its application could be made universal, which we know to be impossible, at any rate in this country. Infected milk is not the only means of attack, and any effective plan of defence must depend upon a thorough knowledge of the enemy's disposition and tactics—a knowledge which we are still far from possessing. While diligently seeking for this further knowledge we shall be wise to assume that the very widespread infection of cattle in this country with *Br. abortus* constitutes at any rate a potential danger to the community which can no longer be safely disregarded. How then can this danger be removed?

The treatment of contagious abortion in cattle is a practical veterinary problem familiar to every veterinary practitioner, but so far, in this country, the object of such treatment has been not the protection of the public from Brucella infection but the protection of the farmer from serious financial loss. That these two aims are compatible can hardly be doubted, or that the veterinary profession as a whole, once it is alive to the issues involved, will join hands with the sister profession in a concerted effort to avert this danger or to remedy the evil which may be disclosed by further investigation. What are the weapons available for such a fight? The inoculation of cattle with living cultures of *Br. abortus* and the elimination of reactors from herds, or, speaking more strictly, the redistribution of animals, guided by the agglutination reaction, so as to reduce the infection of susceptible animals to a minimum.

It is to the dangers incident upon vaccination with live cultures of *abortus* that I wish particularly to direct attention, and to this end I ask three questions:—

(1) In view of the experiments performed by Carpenter and others in the United States in which cattle inoculated with living cultures of *Br. abortus* were found to have become chronic carriers and to eliminate large numbers of the organism in their milk, can such treatment be justified from either an hygienic or a veterinary standpoint?

(2) Supposing the use of live vaccines can be regarded as justifiable in certain circumstances, are they in fact always used for the purpose for which they were originally intended—namely as a prophylactic—or are they not frequently used in a wrong manner—namely as a curative—this practice being encouraged by the farmer's ignorance of the fact that a cow does not usually abort more than once?

(3) Is the use of live vaccines any longer necessary, in view of the success which has been attained in the United States, and on a smaller scale in this country with the elimination of reactors from herds by means of the agglutination reaction? The success of the latter method is testified to by the Committee on Infectious Abortion of the American Veterinary Medical Association, which states in its report that: "Testing Bang abortion disease out of a herd or unit and keeping it out is the only known, successful way to handle it."

(III) *The Origin and Relationships of the Different Members of the Brucella Group.*—It is now generally accepted that this group has special characters, common to all its members, which entitle it to rank as a separate genus. Beyond this point,

however, we launch out into a sea of controversy, some bacteriologists regarding the caprine, bovine, porcine strains (or alternatively *melitensis*, *paramelitensis*, *abortus*, *para-abortus*) etc., as perfectly distinct species, whilst others can find no constant criteria which justify them in regarding the different strains as more than varieties or subspecies of the same species, from which all can be derived by suitable treatment, or produced naturally therefrom under suitable conditions. A remarkable amount of ingenuity has been exercised in the devising of tests, serological, biochemical, cultural, etc., by means of which a classification of the members of the group might be made. These tests appear to me inconclusive and contradictory, but it is too soon to pass a final judgment upon them. I do not doubt that a competent bacteriologist can devise more or less satisfactory means for distinguishing the principal varieties of the organism with which he normally has to deal, but how far does such a classification apply to the varieties encountered elsewhere? Burnet, one of the most experienced and careful workers in this field, reports that he has succeeded in modifying *abortus* strains, by the action of various factors, such as immune sera, antiseptics, bile, quinine, etc., so as to confer upon them all the properties regarded as characteristic of *paramelitensis* strains. *Abortus* he regards as the primitive type of the Brucella group from which both *melitensis* and *paramelitensis* have been derived by the modification resulting from passage through the goat. This question of the origin of the different members of the group is very interesting and, I think, important, because of the light that its elucidation must throw upon the mode of spread of Brucella infections in man and animals. It is a problem which has, however, been very little explored. The view expressed by Professor Eyre in his Milroy Lectures in 1908[1] that "melitensis septicæmia," or as we should now call it, undulant fever, is primarily a disease of the goat, and has accompanied this animal on its world-wide wanderings, has been endorsed by Charles Nicolle, Strachan, Young, and others. But what is the original connection between *melitensis* infection in goats and *abortus* infection in cattle; did the goat infect the cow, or the cow the goat, or were both originally infected from a common but unknown source?

(IV) *Immunity to Brucella Infections.*—Of this aspect of Brucella infections little is known at present. Is there ever a natural immunity to this infection in man or animals?

As regards cattle, there is the interesting fact that a calf born of an infected mother is not usually born infected, though the chorion may be swarming with Bang's bacilli. Moreover, Schroeder and Huddleson have shown that *all* calves appear to be rather resistant to the infection, at any rate for the first three to five months of their lives, and the same appears to be true of kids born of goats infected with melitensis.

Children appear to enjoy a partial immunity of the same kind, those under 5 years of age being seldom affected. This is especially interesting in view of the fact that such immunity is found in countries or districts where a considerable portion of the milk supply is known to be contaminated with *abortus* and one would therefore have expected the children to be more prone to such infection than the adults who, presumably, drink less milk. There is some reason to believe that the children do, in fact, become infected, such infections being too slight to cause recognizable disease, but sufficient to produce some degree of immunity, as positive agglutination and complement-fixation tests for *abortus* have been obtained with from 6% to 17% of the bloods of different series of children examined.

Is there any evidence as to the duration of such immunity inherited or secretly acquired (i.e., without recognizable symptoms of disease) in childhood? I hope that information on this point will be forthcoming. The other point that requires elucidation is whether any lasting immunity is conferred by an attack of undulant

[1] See *Lancet*, 1908, (i), 1677, 1747, 1826.

fever. Sir Percy Bassett-Smith considered that though the evidence of Bruce, Hughes and Eyre showed that some protection was afforded by a previous attack, yet this immunity must be only slight, as second infection undoubtedly occurs. I should like to take this opportunity of paying a tribute to the memory of this able and charming pioneer, to whom all workers in this field owe a great debt of gratitude and under whom I had the privilege of working for a short period.

In conclusion, I hope that this discussion will achieve the important purpose of rousing such an interest in this subject among the members of our professions in general, that large numbers of new workers may join us in this fascinating field. We all hope that systematic investigations may prove that England enjoys a peculiar freedom from undulant fever, but I for one should be pleasantly surprised by such a result. In any case the great problem of contagious abortion cries out for solution, and until this disease has been eradicated a potential danger to the human population will always remain.

Dr. J. T. Duncan : Since the last combined discussion on Brucella infections held by this Society, nearly five years ago,[1] the case against *Br. abortus* as a cause of disease in man has been proved clearly in a great number of counts, and both bovine and porcine varieties of the species have been implicated.

The widespread distribution of the disease brings it within the field of the practising physician in nearly all countries in which epizootic abortion of domestic stock occurs, and for this reason I shall chiefly consider some of the difficulties which confront us in making the bacteriological diagnosis of the disease.

Bacteriological Diagnosis.—Apart from the purely clinical features, the best diagnostic evidence is the recovery of the infecting organism from the blood or urine. In the case of *abortus* infections this is not always easy, frequently it is not possible, and, in consequence, the bacteriological diagnosis in the great majority of cases may depend upon the evidence of agglutination tests with the patients' serum. It is opportune to discuss the value of this test.

Firstly, a positive agglutination reaction, although good enough evidence of Brucella infection, is not, as some writers seem to believe, sufficient to enable us to identify the infecting species, even though the titre of agglutination for one species be higher than for the others. When the agglutinating titre is sufficiently high, more precise information may be obtained from absorption tests with the different species.

One of the chief difficulties in the serological diagnosis of the disease depends upon the alleged occurrence of non-specific reactions. Nègre and Raynaud, in 1911, found that in a series of thirty-nine sera from persons presumed not to have suffered from undulant fever, twenty-two agglutinated *Br. melitensis*. These were regarded as non-specific reactions. Similar observations have been made by many other workers. It is significant that non-specific reactions are said to occur with sera from cases of tuberculosis and enteric fever, diseases in which milk often forms an important part of the diet. Five years before the time of Nègre and Raynaud's observation, Shaw, working on the Mediterranean Fever Commission, examined the blood of 525 apparently healthy dock labourers in Malta and found that in seventy-nine cases the serum agglutinated *melitensis*. Twenty-two of the more promising positives were examined further and *Br. melitensis* was recovered from ten of them. I think that this demonstration of the existence of possibly latent infection throws considerable light on the later observations of Nègre and Raynaud and others on so-called non-specific reactions. It must be borne in mind also that at this time *abortus* infection of man had not yet been recognized.

Another suggestion is that a feeble passive immunity acquired through drinking milk may cause positive serum reactions in uninfected persons; thus, Larsen and

[1] *Proc. Roy. Soc. Med.*, 1925, xix. Joint Discussion No. 1.

Sedgwick, in 1913, found that 17 per cent. of 425 sera from normal American children reacted positively with *Br. abortus*, and this reaction was definitely associated with drinking milk from infected cows. Cooledge and others obtained similar findings and concluded that the reactions were evidence not of active infection, but of a mild passive immunity caused by the absorption of antibodies for *Br. abortus* present in the cows' milk. If this were true, the value of serological tests in the diagnosis of Brucella infections must be very seriously prejudiced.

The question as to whether the serum reactions occasionally met with in apparently healthy persons, depend upon passive or active immunization could be settled quite easily by feeding a group of selected subjects with milk rich in antibodies, but freed from all living *Brucella*, preferably by filtration. Experiments of this kind have been carried out recently by Carpenter. In one of his experiments, six healthy students whose blood showed no agglutinins for *Br. abortus*, drank daily for ten days a litre of pasteurized milk which had the unusually high titre of agglutination for *Br. abortus* of 1 : 1,620. In no case did *abortus* agglutinins appear in the blood, which was tested in dilutions as low as 1 : 3. It must be admitted, however, that the temperature of pasteurization (60° C. for one hour) would almost certainly destroy some of the agglutinins. Apparently Carpenter guarded against error by re-examining the milk after pasteurization. The experiment is worth repeating. In support of Carpenter's findings there seems to be some evidence that the incidence of human reactors to *Br. abortus* is lower in towns served with pasteurized milk than in those in which untreated milk is used.

I think enough has been said to cast some doubt on the importance of non-specific reactions in the serological diagnosis of Brucella infections.

In the past, before *abortus* infection of man was recognized and non-specific reactions were thought to be common, different workers fixed the safe minimum diagnostic titre for the agglutination test at figures based on their individual experience. These titres varied from 1 : 200 (recommended by Fici) to 1 : 10 (recommended by Nicolle); the majority favoured titres of 1 : 80 to 1 : 100. At the present day a minimum titre of 1 : 100 is required in the diagnosis of *Br. abortus* infections in Denmark.

Consider for a moment the maximum titres of agglutination which may be met with in proved undulant fever. Although titres of 1 : 5,000, 1 : 10,000, or even 1 : 20,000 are occasionally recorded, very low titres, as low as 1 : 40 or 1 : 80, are not uncommon, and this is especially true in cases of severe infection. Burnet states that 20 per cent. of cases of undulant fever develop no agglutinins, and this experience has been confirmed by others.

It is clear, therefore, that by fixing the minimum diagnostic titre as high as 1 : 100, serious omissions in diagnosis may follow. For example, in 296 cases included in a recent report only 11 sera gave agglutination titres for *Br. abortus* of 1 : 100 or over, 283 were under 1 : 50, and 209 were 1 : 15 or under. So that a minimum diagnostic titre as low as 1 : 50 would have failed to detect 95 per cent. of these 296 cases.

Briefly, there is little reason to believe that non-specific reactions are of common occurrence. On the other hand, it is clear that latent infections may occur with marked agglutination reactions but no clinical symptoms, and also, occasionally, in clinically and bacteriologically proved cases of undulant fever the agglutination reaction may be very feeble or totally absent. In view of these facts I think it is necessary that we should revise our ideas of what may be accepted as the safe minimum diagnostic titre. Using trustworthy suspensions of the appropriate species and taking precautions to guard against error arising from the prozone phenomenon, I think a fairly low titre may be accepted with safety.

The agglutination tests should be carried out at a temperature of 37° C. to 40° C., maintained for a few hours, and final readings taken the following day. The common practice of heating the serum to 56° C. for thirty minutes, to destroy

the so-called non-specific agglutinins, should be avoided; such a temperature may lower the titre of a specific serum or even, in rare cases, totally inactivate it.

Identification of Brucella Types.—Specific differences—if they can be called specific differences—are very slight and are apt to be inconstant. Morphologically, in most circumstances, the species are indistinguishable from one another, but under favourable conditions of cultivation, such as the early growth on a rich blood digest agar, the *abortus* types may develop bacillary forms reaching a length of 2·00 μ to 3·00 μ, while *Br. melitensis* remains coccal or very rarely exceeds 1·00 μ in length. Bang gave the length of *B. abortus* as up to 3·00 μ, and this size is also given by Schroeder and Cotton, and Mohler and Traum, but Fabyan, with a great experience of *Br. abortus*, states that rarely did he find it to reach a length of 1·50 μ. It may be said, then, that a Brucella measuring 2·00 or 3·00 μ in length is very probably, if not certainly, *Br. abortus*. Morphology is a feature which has received too little attention in the study of this group.

In contrast with the case of *Br. melitensis*, the primary cultivation of bovine *Br. abortus* is somewhat difficult and the organism requires an atmospheric carbon dioxide tension of 5 to 10 per cent. during a variable number of transfers. In its need of additional carbon dioxide, bovine *Br. abortus* differs from all the other Brucellas, including the porcine variety and the Rhodesian bovine strains. It is the inability of fresh strains of normal bovine *Br. abortus* to develop in unsealed tubes in ordinary air that distinguishes this variety. Therefore it is necessary, when attempting to cultivate the organism from man, to provide a suitable carbon dioxide environment for some of the cultures. If other methods fail, direct inoculation of guineapigs should, if possible, be resorted to.

In the identification of the Brucella species there are three differentiating methods in common use; these depend upon the liberation of hydrogen sulphide from media, the bacteriostatic action of certain dyes, and serological distinctions.

(1) Huddleson has drawn attention to the fact that on a liver infusion agar medium of slightly acid reaction and rich in organic sulphur, the *abortus* varieties liberate a considerable quantity of hydrogen sulphide within from twenty-four to forty-eight hours at 37° C., while recently isolated *melitensis* strains fail to liberate any, or liberate only a very slight amount. The distinction, however, is not always sharp, and the test suffers from the defect that the particular medium recommended is not capable of standardization and the quantity of hydrogen sulphide formed will vary with the available organic sulphide content of the medium. In addition, a better method of measuring the quantity of hydrogen sulphide than by the use of lead acetate paper is desirable. Under standardized conditions, however, this test might prove of value and in any case it should repay further study.

(2) The bacteriostatic action of dyes: Following the work of Churchman, Huddleson and Abell showed that the Brucella species differed in their resistance to the antiseptic action of methyl-violet. Briefly, it is stated that a concentration of 1 : 100,000 of methyl-violet in a solid medium permits the growth of *Br. melitensis*, retards that of bovine *Br. abortus*, and totally inhibits that of porcine *Br. abortus*. An examination of the published tables, however, shows some overlapping of bovine *Br. abortus* by feeble resistant *Br. melitensis* strains, and of porcine *Br. abortus* by bovine. Huddleson has recently stated that basic fuchsin in a concentration of 1 : 50,000 inhibits the growth of porcine *Br. abortus* but not bovine *Br. abortus* or *Br. melitensis*, and another dye, thionin, in similar concentration inhibits bovine *Br. abortus* but not porcine strains or *Br. melitensis*. Confirmation of this work is awaited.

On the whole, the method of dye bacteriostasis is a notable advance in the differentiating tests, but these tests demand the most accurate standardization of the dyes employed. Like the foregoing, it is a method which should repay further study.

(3) Serological differentiation. By the agglutinin-absorption test the Brucella organisms may be arranged in a number of groups; Miss Evans has recognized eight such groups. Some of these are fairly sharply defined and the species pure, but others are poorly defined, and although pure *Br. melitensis* groups have been found, the *Br. abortus* groups are overlapped by apparent *Br. melitensis* strains. These discrepancies may have arisen in some measure from the use of old strains unsatisfactory for purposes of serological study, strains of uncertain origin or strains from human sources which were labelled "*M. melitensis*" at a time when abortus infection of man had not yet been recognized.

The last word on serological grouping of the species has not been said. Serological distinctions are sufficiently marked to justify further study starting *de novo* with freshly isolated authentic strains specifically identified as far as possible by the other means available.

Amongst other differentiating tests, the method of Ficai and Alessandrini, based on the alleged greater thermal stability of agglutinins specific for *Br. abortus*, and that of Vercellana and Zanzucchi, depending on the greater susceptibility of *Br. melitensis* to flocculation by dilute solutions of lactic acid, have proved untrustworthy.

Regarding animal experiments, the *Brucella* species undoubtedly exhibit differences in their virulence for particular animals. Time will not permit a discussion of this subject, but it should not be overlooked that individual strains of a species may also exhibit differences in virulence.

It will be seen that although a great deal of work has been done on the differentiation of the *Brucella* group, much remains to be done, chiefly in perfecting methods already in use.

Epidemiology.—With regard to the epidemiology of *Br. abortus* infections of man, infection by both bovine and porcine varieties of *Br. abortus* through contact with sick or aborting animals, or their carcases, has been proved in many cases, but the great majority of infections cannot be traced to any such mechanism. Suspicion points strongly to cow's milk as the vehicle of infection, but the peculiar sporadic distribution of the cases makes proof of this difficult. To quote Bevan's experience in Rhodesia: "It rarely happens that more than one member of a family is affected, and in at least two instances, residents on infected farms have escaped, while a visitor, or a recently arrived farm pupil, has become infected."

Except that the disease is rare amongst young children, age, sex, and occupation seem to bear no relation to its incidence. In determining the sporadic distribution of the cases, it must be remembered that only those of clinically manifested disease have been taken into account, and no real attempt has been made to determine the incidence of infection, because the possibility of latent infection seems to have been overlooked.

Individual susceptibility both to infection and to clinical disease may play a part. With the more virulent *Br. melitensis* infection some persons develop a very severe relapsing disease extending over two, five or even seven years, sometimes with long latent periods, others exhibit only a comparatively mild disease ending in apparent recovery after a few months or even weeks, and others still, as shown by Shaw, may present no clinical manifestation whatever.

It is reasonable to assume that the less virulent *Br. abortus* may give rise to similar mild cases and latent infections, and for this reason it is desirable that when a case occurs in a family, the other members of the household or other persons similarly exposed to the milk infection should, if possible, be examined bacteriologically or serologically. In this way we may obtain more accurate data regarding the distribution of the infection.

It is a fact that in the United States, Denmark, England and elsewhere, large numbers of sera from cases not previously diagnosed as undulant fever have been

examined, and a variable percentage found to agglutinate Brucella organisms. These sera, collected primarily for the typhoid Widal or the Wassermann test, were presumably morbid, and it is amongst the negatives from these tests that we should seek reactors to *Br. abortus*. It was in this way that the widespread distribution of abortus fever in Denmark and elsewhere was brought to light. In Harrison and Wilson's series in England 5·41% of 998 Wassermann negative sera reacted with *Br. abortus* in titre of 1 : 10 or higher. Researches of this kind should be conducted in all areas where epizootic abortion of animals is known to occur, and, whenever possible, a bacteriological examination of reactors should be made with the object of recovering the infecting organism. For purposes of comparison or to detect latent infections, mass examinations of sera from apparently healthy persons using unpasteurized milk in areas where the animal disease exists, should be carried out; senior school children or inmates of institutions might be suitable subjects.

Is this Disease a New One?—The question is asked frequently, "Is this a new disease, or merely one that has been unrecognized in the past?" I think that the evidence does not tend to support the assumption of a new, and consequently progressive, disease. In nearly all countries where epizootic abortion of domestic stock is rife a very diligent search has revealed the existence of human infection. On the other hand it is difficult to believe that a disease so closely allied to Mediterranean undulant fever, with its striking clinical features, could have remained so long unrecognized. The *abortus* fever in Europe and America, so far as the published reports inform us, in all but a few cases seems to present a much less severe clinical picture than that of the Mediterranean disease.

However, deaths from *abortus* infection have been recorded from Rhodesia, the United States and Denmark: in the last-named country with 500 cases reported annually, the death-rate from the disease is between 2% and 3%, that is, about the same as in Mediterranean undulant fever.

That the disease is increasing in certain countries, such as Rhodesia and the United States seems to be true, but in these instances the human infection has merely followed the overflow of the animal disease into new areas, and it is significant that in both of these countries the porcine variety of *Br. abortus*, or a type very closely resembling it, seems to be largely responsible for the disease in man, even though the cow is the actual source of infection.

Mr. L. P. Pugh: I wish to say a few words in connection with the animal side of the subject under discussion, more especially with reference to the vexed question of the use of live cultures of *Br. abortus* in the handling of outbreaks of contagious abortion in cattle. Whether future evidence will justify the continuance of the use of live vaccine is difficult to predict at the moment; but I hope to show you the reason why the Ministry of Agriculture and veterinarians have employed this form of vaccination and the justification for that use.

In order to illustrate my points I will quote some of the conclusions that Captain Dalrymple-Champneys drew from the evidence he collected:—

(5) Contagious abortion of cattle is known to be extremely prevalent in this country, though no statistical evidence as to its incidence is available, and it is the cause of very serious financial loss to cattle breeders.

(6) It is known that cows infected with contagious abortion often become chronic carriers of the infective organism (even though they may never abort), and continue to excrete it over very long periods in their milk, either continuously or intermittently.

(8) The treatment of infected herds by vaccination with living cultures of *Br. abortus* is very popular in some countries, and is generally regarded as having a prophylactic value in certain cases, but there is evidence suggesting that this practice may not be free from danger, since the animals so infected, may become chronic carriers of the disease, and continue to excrete the infective organism in their milk over long periods. The policy of cleansing herds of contagious abortion by the elimination and exclusion of reactors to the

agglutination test has proved very successful, both in this country and in America, entirely free from danger, and is considered by many observers as being preferable to vaccination.

It is certainly true, as Captain Dalrymple-Champneys has said, that *Br. abortus* infection of cattle is very common in this country; many competent observers estimate that over 80% of our herds have the disease, either in an active or else in a chronic form. The losses, direct or indirect, can be counted in millions of pounds and may be classified roughly under the following heads: (1) Loss of calves. (2) Loss of milk. (3) Loss of life, bodily condition, etc., as a result of metritis and other septic sequelæ. (4) Losses due to sterility. (5) Loss due to replacements, to keep up milk contracts.

The greatest loss is occasioned through septic sequelæ leading to sterility, and it is a loss which is the least apparent to the outside world.

The Ministry of Agriculture recommends that when the disease is proved in a herd, the affected animals should be isolated and the rest of the cattle subjected to the agglutination test, all reactors to be isolated and treated as a separate unit. If, however, this method fails, or if the disease has a firm hold, then they recommend the use of a live culture of *Br. abortus* given subcutaneously at such a time that the organisms are not likely to take up their position in the uterus, i.e., heifers are inoculated six to eight weeks before pregnancy, and cows are treated as soon as the puerperal period is over.

In practice it has been the general experience of breeders and farmers that losses coming under the afore-mentioned headings are very greatly reduced, so that the farmer can be promised with a good deal of assurance that he will have a regular supply of calves and milk if live vaccination is carried out. From an economic point of view this assurance is most important and valuable, and once a farmer has had experience of treating a herd by this method he will seldom go back to the more hazardous method of isolation.

The farmer, unfortunately, cannot follow the counsel of perfection advocated by wealthy herd owners in this country and in America, i.e., to eliminate all reactors. It is certainly true that a herd can ultimately be cleared of *Br. abortus* infection by the continuous application of the agglutination test, and the ruthless elimination of reactors, and as Captain Dalrymple-Champneys says, it is certainly safe—to the eliminator. But what is to be done to the reactors? An owner of cattle, unless he is a philanthropist, cannot butcher his best milch cows because they happen to harbour *Br. abortus* It can be taken as almost a certainty that, if a farmer decides to get rid of reactors, the latter will ultimately find their way into the open market and so enter other herds.

I believe the elimination of *Br. abortus* infection of cattle in this country by isolation and destruction of reactors to be economically impracticable, more especially when one considers the fact that schemes are being discussed at the moment for the destruction of all tubercular cattle.

Captain Dalrymple-Champneys points out that the abortion rate in a herd automatically falls in the second and third years of an outbreak. This is certainly true up to a point. But what about all the young heifers and cows coming along in the presence of so many "carriers," and what of the freshly imported cows, brought in to make up the wastage of the first year of the outbreak? Of course they contract the disease, and as the outbreak wears on (and incidentally wears out the farmer) so increases the virulence of the secondary septic organisms that gain entrance to the uteri of aborters, and sets up various forms of metritis. So virulent at times do these in vaders become that even if cows calve down normally on these premises, they fall victims to puerperal infection of a more or less serious nature, and sterility follows.

Quite apart from these arguments, I do not believe there is any evidence to suggest that more carriers result from the artificial inoculation of the organism than result from a natural outbreak of the disease in a herd.

There is a good deal of evidence to suggest that it is the actual handling of infected material that is likely to be the source of danger to human beings. The discharge from an aborting or recently aborted cow is by far the most dangerous in this respect. If, therefore, by the judicious use of a live vaccine one can prevent this accident and render the animal in such a state of immunity that she only eliminates the organism in relatively small numbers, surely this procedure must receive the approval of those responsible for the health of man rather than the reverse.

There is one further constructive suggestion that I would like to make. When a cow is inoculated with the live vaccine, she may possibly eliminate the live organisms in large numbers in her milk and urine for a number of days. If on investigation this should prove to be the case, then it would appear necessary to control inoculated animals for the number of days that would be determined by such an investigation.

Brucella infection of pigs appears to be uncommon in this country at the moment, but in view of what the essayists have said to-night, I think that closer search may reveal that the disease is more prevalent than is at present apparent. Such an investigation is imperative, since judging from American findings it would appear that the porcine strain of *Br. abortus* is more pathogenic to man than the pure bovine strain.

In conclusion, therefore, I put forward the following points for consideration :—

(1) That there is no evidence that the number of *Br. abortus* "carriers" will be greater following vaccination than would result from the natural disease.

(2) That the complete elimination of reactors to the agglutination test for *Br. abortus*, from herds in this country, is economically impracticable.

(3) That vaccination with the live organisms at the correct period is, from the owner's point of view, the soundest policy to adopt in seriously affected herds.

(4) That live vaccination, by preventing the majority of abortions, and therefore the handling of highly infected material, will tend to protect human beings from the commonest source of massive infection.

(5) That investigation of the immediate fate of the live organisms injected should be carried out, as there may be a serious elimination of organisms from the cows immediately following this procedure.

Dr. P. Manson-Bahr said he had had experience of seven cases of undulant fever contracted from goat's milk in the tropics or subtropics during the last eight years, and during that period had seen three cases of "abortus fever" in man. His contribution to the discussion could only be from the clinical aspect, and his impression was undoubtedly that *abortus* fever was a much milder disease and ran a much shorter course, terminating usually in the third or fourth month; whereas as was known, undulant fever was protracted for a year or more. He thought that the initial symptoms might be different in *abortus* fever. In the cases he had seen, pain on lateral movement of the eyes, pain in the alveolar margins of the jaw, parotitis and orchitis were in evidence as prodromal symptoms. So much so that one patient was fitted with new glasses by his oculist, and had several teeth extracted by his dentist, while his case was finally diagnosed as one of "testicular mumps"!

He (the speaker) had tried a number of methods of treatment, but was not convinced of the benefit of any particular one. With regard to vaccine treatment it was necessary to keep an open mind. His own belief was that it tended to modify the disease, but not to shorten its course. As regards diagnosis, he had found the intradermal test of Burnet, or the "melitene" reaction, of distinct value.

Dr. G. S. Wilson said that the distribution of *abortus* fever in this country might be wider than was generally supposed. In Denmark, Kristensen had examined 6,505 Wassermann sera by the complement-fixation reaction, taking a positive

reaction in a serum dilution of 1/20 as suggestive of infection with *Br. abortus*; of these sera, thirty-one, or 0·48%, had reacted positively. In this country Harrison and Wilson had examined 998 Wassermann sera by the agglutination test and had found that 7, or 0·7%, agglutinated *Br. abortus* to 1/80 or over. Again, Kristensen had examined 4,623 Widal sera, and found that 500, or 11%, agglutinated *Br. abortus* at 1/100 or over; while Harrison and Wilson in this country, examining fifty-two Widal-negative sera, had found that six, or 12%, reacted to 1/80 or over. These figures suggested that infection with *Br. abortus* might be as widespread as in Denmark. The epidemiology of the disease was very puzzling; most of the clinical cases occurred in young men—an incidence quite different from what one would expect if the disease was usually contracted by drinking infected milk. Kristensen had obtained evidence to suggest that the majority of the cases were due to direct infection from contact with aborting animals, and not to indirect infection from consumption of milk. Since about 9% of samples of milk in one part of this country were found to contain *Br. abortus*, it seemed probable that many children must become infected with this organism, though the infection did not appear to give rise to clinical symptoms. To ascertain the extent of this latent infection it might be advisable to examine the glands of a series of children dying from various causes

Dr. Tom Hare said that there was a division of opinion in the veterinary profession of Great Britain to-day as to the best prophylaxis of contagious bovine abortion, which was thought to be the most widespread bovine disease in the country. Supporters of the use of live "anti-abortion vaccine," as Mr. Pugh had so ably shown, were able to justify their policy as a means of saving the money of one type of stockowner. Vaccination, however, was antagonistic to the interests of the pedigree stockowner, who was required to keep his herds free from the disease, whether it was naturally or artificially acquired; to such owners the policy of the hygienist was the best business proposition. Discussion upon these mutually destructive policies would not answer the fundamental question, viz.: Had the live vaccine reduced the incidence of contagious abortion in Great Britain?

This vaccine was introduced and recommended some fifteen years ago by the Ministry of Agriculture as the *best* preventive of bovine contagious abortion. In spite of doubts entertained by certain qualified judges as to the reliability of the Ministry's field experiments, and in spite of the greater part of the veterinary profession being unprepared to understand the application of the vaccine, the Ministry found it expedient to satisfy the clamour of agriculture that something should be done to save their pockets. He maintained that the Ministry of Agriculture was not above criticism for having failed accurately to observe the effects of their action. However, since the Ministry had not provided the country with indisputable statistics, it was not possible to determine whether active immunization by means of the live vaccine had reduced the incidence of the disease in Great Britain.

He suggested the desirability of encouraging the Minister of Agriculture to institute such inquiry as would provide the country with indisputable information as to the incidence of the disease and the best means of preventing it. If Captain Dalrymple-Champneys' prediction proved substantially well-founded, that in Great Britain infection was conveyed to man through contact with diseased animals or their products, then the information required from the Minister of Agriculture would be of as vital interest to the medical as to the veterinary profession.

Dr. E. W. Goodall said that most clinicians with lengthy experience of acute infectious diseases in this country had met with cases of continued fever which had puzzled them. Sir James Goodhart published a paper in the *Guy's Hospital Reports*[1] forty-one years ago on such cases under the title of "Innominate Fever,"

[1] *Guy's Hospital Reports*, xlv (S. 3, xxx), 379.

and some of the cases and charts given in that paper might well be those of Brucella infection. There could be little doubt that the infection had been present in past times, and had been diagnosed as "typhoid," "influenza," "continued fever," and so forth. How long did the agglutinins persist in the blood and could the absence of agglutinins be taken as evidence that a person had never suffered from a Brucella infection? Was there any clinical evidence of mutual immunity between *Br. melitensis* and *Br. abortus* infection, as there was between typhoid and paratyphoid? He thought that more would have been said as to the method of dissemination of the disease. In the discussion attention had been directed chiefly to milk infection.

In the *Journal of Infectious Diseases* for October, 1929, xlv, 271, there was a paper by Hardy, Hudson and Jordan, entitled "The skin as a portal of entry in *Br. melitensis* infections." The authors had investigated the occurrence of the disease in Iowa, U.S.A., in a factory for making sausages and similar articles of food from pigs, in which about 3,500 pigs were killed daily. There was evidence that contagious abortion occurred in those animals. The infection was met with most frequently amongst those employees who were engaged in killing the animals and cutting up the carcases, that is in handling fresh tissues and organs. These authors also found that the cases of undulant fever occurring in that neighbourhood amongst farm-workers were chiefly amongst the males, that is, those persons who were specially likely to handle infected animals. In milk-borne infections the evidence was about the same in males and females, so that a person's occupation might be a factor in the incidence. The authors had also carried out certain experiments in guineapigs, which bore out their contention that infection might be conveyed through the abraded skin.

Dr. J. D. Rolleston said that though he had had no practical experience of undulant fever, he had in his capacity of medical superintendent of a fever hospital taken a considerable interest in the disease for some time and had recently summarized the literature on the subject from British and foreign journals.[1] Although he had had nearly thirty years' experience of fever hospital work, he could not recall any case whose course corresponded to the descriptions of undulant fever. Dr. J. E. MacCartney, the director of Pathological Services of the Metropolitan Asylums Board, had just informed him that though it had been the practice for the last eighteen months to examine for agglutination of *Br. abortus* all the serums sent from the Board's hospitals for the Widal reaction, there had been only one case in which such an agglutination had been obtained, but it was of very short duration, as in the following week the result was negative.

As a former President of the Section for the Study of Disease in Children, he had been particularly interested by the fact, to which Madsen,[2] of Copenhagen, among others, had drawn attention, that the members of the community who consumed most milk, namely young children, were immune to the disease.

Captain S. R. Douglas said that laboratory infections from *B. melitensis* were very common; he had personal knowledge of more than a dozen. In the case of *Br. abortus* derived from cattle, laboratory infections, if known, were apparently very rare, in spite of the fact that large amounts of vaccine containing living organisms were manufactured and distributed in this country. Recently, however, American workers had shown that strains of *Br. abortus* derived from swine frequently caused laboratory infections in man. It therefore occurred to him (the speaker) that light might possibly be thrown on the problem of human susceptibility by experiments on monkeys. For instance, it might be well worth while to ascertain if porcine strains of *Br. abortus* still retained their infectivity for monkeys after being passaged through cattle.

[1] *Bulletin of Hygiene*, 1929, iv, 512-516.
[2] *Bull. Office Internat. d'hyg. publ.*, 1928, xx, 1395.

Captain Dalrymple-Champneys (in reply) said that the interesting discussion had more than fulfilled the objects at which he had aimed in his opening paper. They had heard the question of the control of contagious abortion set forth in a most interesting manner by experienced veterinarians with different view-points, and though one of these had, he felt, gone rather beyond his convictions in order to show that the use of live vaccines could be defended, yet he (the speaker) was extremely glad that this view had been presented. He welcomed Mr. Pugh's support of his proposal to investigate the possibility of contagious abortion among swine in this country, an investigation which he thought might have important consequences.

JOINT DISCUSSION No. 3.

Section of Psychiatry, and Section for the Study of Disease in Children.

[*December* 10, 1929.]

DISCUSSION ON THE DIFFICULT CHILD.

Dr. Bernard Hart: "The difficult child" is a term which covers a very wide field. It includes on the one hand a great range of behaviour anomalies, from trifling bad habits up to the most serious forms of delinquency, and on the other hand such heterogeneous "nervous" phenomena as timidity, defective sleep, refusal of food, enuresis, and night-terrors. It is not easy to find an adequate definition to cover so extensive a sphere, but one couched in biological terms will perhaps be the least objectionable.

If we regard the aim of nurture and education of children as the acquirement by the child of the faculty of adaptation to the environment in which it has to live, then the difficult child may be defined as one who presents obstacles to the achievement of this aim.

The difficult child has always been known, and has always constituted a problem for the parent, the educator, and the doctor, but the hypotheses held as to the causation of the difficulty, and consequently the lines along which a remedy has been attempted, have changed considerably in the course of recent history. This change may be said to have progressed from an ethical view-point to a physical, and thence to one predominantly psychological and biological.

Formerly the only explanation attempted lay in the assumption of a congenital weakness of moral fibre and an extra dose of original sin, and treatment was limited to exhortation and discipline. This hypothesis has hardly survived except with regard to that very unsatisfactory and puzzling group of cases which we include, mainly as an expression of ignorance, under the term "moral imbecility." Then came the period when the difficulty was ascribed to some disease or deficiency in one of the bodily organs, with a resultant obstruction in the task of adaptation to life and its environment. A long list of causes has been put forward here, ranging from factors of doubtful potency, such as teething and threadworms, to conditions of unquestionable importance such as septic tonsils and adenoids. Investigations along such lines have produced, and continue to produce, knowledge of the utmost value in the understanding and treatment of these cases. There can be no doubt, however, that causes of this kind often play only a secondary part, that they rarely afford a full explanation of the picture before us, and that if the investigator's attention is concentrated too exclusively upon such factors, a failure of perspective and of adequate understanding is inevitable.

The next conception with which we have to deal is that of the "nervous child"—the view that the anomalies of behaviour and reaction shown by the cases with which we are here concerned are a manifestation of the same kind of disturbance as that met with in functional nervous disorders, and indeed that the difficult child is likely to become the neurotic adult. This conception, like that of functional nervous disorders in general, had at first a physical colouring, and the explanation of the phenomena was sought in some anatomical, physiological, or chemical anomaly

in the nervous system. Here again a definite advance in knowledge and understanding was attained, in that emphasis was laid upon the soil in which the weeds of "difficulty" grew, and not merely upon exciting causes of the order of tonsils and adenoids.

The view which we may designate as the most modern, and perhaps the most adequate, has developed from a change in the conception of the nervous child, a change which has been consequent upon that which the conception of functional nervous disorders has itself undergone. These disorders are no longer regarded as diseases of the nervous or of any other single system, but as faulty reactions of the individual as a whole. In these reactions, as must necessarily be the case where reactions of the individual as a whole are concerned, psychological factors have to be taken into account, and the disorders can only be adequately understood if psychological conceptions are brought to the aid of physical and chemical conceptions. In other words, the disorders which used to be called functional nervous disorders, but are becoming more commonly known now as the psychoneuroses, are regarded from a psychobiological viewpoint, and the part played in them by psychological processes is held to be of essential and dominant importance.

This conception of the psychoneuroses as faulty reactions of the individual to the internal and external circumstances in which he has to live has been extended to the problem of the nervous child. The various symptoms which he displays are considered to be due, not merely to disease of any particular organ or system of organs, but to a fault in the child's reaction as an individual. They cannot therefore be understood unless the psychological situation is taken into account, although all factors of the order of disease or organic insufficiency must of course be given their due weight.

The "difficult child" is a term covering a wider field than the "nervous child," and includes all kinds of anomalies in behaviour which do not obviously come under the latter heading. In particular we have to include here the phenomena of delinquency, ranging from such minor manifestations as truancy up to serious forms of anti-social conduct. Nevertheless, once the conception of a failure of psychobiological adaptation is adopted, it is clear that all these conditions have as much claim to be brought under it as those of "nervousnesss," and that they require investigation and treatment along similar lines. The actual association of such anomalies of behaviour with definitely nervous symptoms is, of course, a clinical commonplace.

The modern and most fruitful view of the difficult child is therefore to regard him as a problem in behaviour, and to consider the symptoms he presents as reactions to the internal and external circumstances of his life. These circumstances must be considered essential from a psychological standpoint, but not exclusively, because a due appraisement of the child's physique, particularly the presence of definite disease or organic insufficiency and the manner in which such factors may be influencing the total reaction, is absolutely necessary to adequate comprehension.

If this conception is correct it is apparent that in order to understand and to treat the difficult child and the reactions which he is displaying, we must know a great deal about himself and the environment in which he has to live. We must know his physical and mental make-up, and any factors of either order which may have a bearing upon the question at issue. We must know also the circumstances of his life at home and at school, and something of the people with whom he comes in contact in both these environments. Moreover, if we find that the "difficulty" which has arisen is the result, not merely of internal factors in the child's mental and physical economy, but also of a faulty attitude or practice on the part of parents, teachers, or companions, then we must have some means by which we can get into contact with and modify those external agencies.

This is a formidable task, and one which could hardly be dealt with adequately by a doctor working single-handed, even if he had the necessary time to devote to it. Under the conditions usually holding in a hospital out-patient department it is of course altogether impossible. It is obvious that, if the problem is to be satisfactorily attacked, some kind of organized team work must be employed. An organized team attack of this character constitutes the essential feature of the child guidance clinic which, originally developed in America, is now making its appearance in this country.

The fundamental machinery of a child guidance clinic consists in the employment of a team of at least three persons, a psychiatrist, a psychologist, and a social worker, who investigate the child and its environment from their respective standpoints, collate and modify their results by one or more joint conferences, and finally carry out a line of treatment designed to remove the causal factors which have been elicited. The psychiatrist is the head of the organization, superintends its activities, and provides the necessary medical scaffolding into which all the work has to be built. The psychologist investigates the mental make-up, and the directions in which this is being strained or made to work inefficiently by the educational and other processes to which the child is being subjected. The social worker, who has received a special and lengthy training in order to fit her for a task which is by no means easy, has to make herself acquainted with the environment in which the child lives, the parents, home conditions, teachers, and so forth, and a large part of the treatment, in so far as that involves an attempt to modify those environmental factors, necessarily falls to her lot.

Such a scheme is open to many obvious criticisms. Team work of this kind is always somewhat repugnant to the clinically-minded physician, who feels that that intimate relationship which can only exist between a patient and his doctor, and which often constitutes an indispensable basis for therapy, must be lost when the doctor is replaced by a team, even although an attempt is made to weld the team into a unity by the procedure of the conference. Moreover, the important part in subsequent treatment which necessarily devolves upon the social worker must tend frequently to displace the physician from an actual to a titular headship, and to lead to the social worker tail wagging the psychiatric dog. I hasten to add, however, that those of us who have had the privilege of experiencing the immense help which an efficient social worker can afford us in the treatment of psychiatric cases will readily agree that this risk is well worth taking.

Real though I believe these objections to be, the problem is of such a character that they cannot be completely avoided, unless we are to content ourselves with the old individualistic method of approach, with all its obvious inadequacies. The American scheme has been rationally conceived, it has already proved its value, and with careful development and a consistent avoidance of that tragic "running before we can walk" which so often wrecks promising new methods, it should prove of great value in the management of a supremely important class of case.

Dr. Hector Cameron: When we study the difficult child we must concede that he is also a problem in pure pædiatrics, although nothing that I have to say on that side must be taken as appearing to show that I undervalue the importance of the contribution made by psychiatry to the subject.

The "difficult" child we know well: eager, thin, pale, wasting his little body with the intense energy which he puts into the whole business of life; a bad sleeper, a notable refuser of food, often squinting or stammering, or incontinent of urine, and especially subject to certain strange "bouts" or "turns," or "attacks" as the mother calls them, marked by increase of pallor, by prostration, by a furred tongue, foul-smelling breath, constipation, irregular pyrexia, and so forth. My purpose is, rather, to stress the ætiological significance of this metabolic instability

in the disordered conduct of the child. Often in childish disorders it is hard to know what is cause and what is effect. A sleepless, restless state in an infant produces hunger, and hunger produces the restless state. Faulty nutrition lowers resistance against catarrhal infection, yet catarrhal infection is a main cause of faulty nutrition. Here the difficulties of life, the irritable opposition, the unrest, produce the metabolic disturbance, yet, whenever metabolic disturbance is present, there is apt to be an exacerbation in the symptoms of unrest.

The intolerance of the hypersensitive difficult child for fat is well recognized. The biochemist tells us that the energy expended upon muscular exertions and upon emotional activity is derived, in the first place, from the circulating carbohydrate in the blood. Of carbohydrate the body has but a meagre reserve, stored in part in the liver and in part in the muscles. Great emotional excitement, great exertion, or any transitory infection is capable of lowering the available carbohydrate reserve, and the body is then forced to draw more and more upon its main reserve of energy, its stored body fat. With insufficient carbohydrate the metabolism of fat is imperfectly achieved, and intermediate products of that metabolism are apt to accumulate in the blood. A state of ketonæmia results. Pallor, vasomotor anæmia, amyotonia, low blood-pressure, fainting, a low blood-sugar, nausea, constant yawning or sighing, a smell of acetone in the breath, an irregularity of the temperature curve and vomiting are, I suggest, the physical accompaniments of this disturbed metabolism. It is the state which Osman, in describing what he calls debility in childhood, has named glycopenia. In many cases vomiting is the most prominent symptom. We are then confronted with the picture of cyclical vomiting. But very often, with symptoms otherwise identical, vomiting is only occasional, or altogether absent. Not all children suffering from what is graphically called "home sickness" actually vomit. In this condition we can, I think, recognize a certain emotional state as characteristic: opposition, irritability, tearfulness, apprehension, terror, loss of confidence, loss of the power to concentrate are mental states corresponding to the physical state. The schoolmaster, as a rule, less apt to be impressed by the pallor and the general air of lassitude which distresses the mother, notices especially a deterioration in the power to concentrate, sometimes amounting to a state of confusion. We cannot but be reminded of the mental states, similar or more profound, which are characteristic of insulin hypoglycæmia.

I do not want to do more than stress one aspect of the question. There are cases in which the attack must be, in the first place, due to metabolic disturbance, which must be corrected before psychiatry can meet with much success in controlling conduct. A readjustment of the diet, with more sugar and less fat, and with glucose given freely at short intervals, has often been of real service. Glucose at bed time seems especially helpful. These eager, restless children seem to stand even the normal sugar shortage of the night badly. Herein may be in part the explanation of the restless nights, with moaning, night-terrors, enuresis, etc., and I think it is certainly the explanation of their unhappy state in the early morning. So many of these children "get up on the wrong side;" they lose their school pencils before they go to school; there is fuss, worry, irritation over little difficulties, which later in the day they are able to overcome.

I stress this aspect of the problem because it seems to me to show the need for pædiatric control in the treatment of the difficult child.

Dr. William Moodie (Child Guidance Council): The child guidance clinic is one in which the special team method of observation and treatment is carried out. The name is rather an unfortunate one, because it suggests to the layman some sort of interference with the upbringing of children, and the average parent resents any suggestion that he is not in every way capable of carrying out this function without external aid.

The team method, originally evolved on somewhat theoretical grounds, has proved to be practically useful in its employment in many clinics in America, and also, to some extent, in this country. Its original evolution resulted from the discovery, on the part of those who deal with behaviour problems in children, that these could best be tackled from four aspects, physical, temperamental, intellectual and environmental. The psychiatrist examines the physical condition and the temperament; the psychologist, the intelligence of the child; and the social worker his history and environent. In some clinics a fourth person is added, a pædiatrician, who reports on the physical condition, instead of the psychiatrist having to do so. This method is of course cumbersome, and costly, and worthy of adoption only if the advantages prove in practice to repay the extra expense and complication. There are also certain disadvantages. It will be well, then, for us to consider these in detail.

In child problems above all, an accurate past history is essential. This can to some extent be obtained by the doctor in his consulting room, and a description of the environmental situation in the home may also be obtained by the doctor in the same way, but unless he is dealing with private patients whom he visits in their own homes, this must be given by the adult concerned. In obtaining this history, both as regards past illnesses of the patient and the environment in the home, the social worker is not only frequently of great assistance, but in some cases indispensable. Descriptions given by parents, especially by unintellectual parents, are frequently wrong, and always confused, so that it takes a great deal of the doctor's time to arrange the facts in order. This work can be done just as accurately by a trained social worker, whose time is not so valuable. Much mishandling by parents is, moreover, the result of depressed attitudes acquired during their own childhood, and therefore, with the best will in the world, the parent is incapable of supplying information which may be of great importance. In such cases the social worker can visit the home in a friendly and unceremonious way, and can see how the child behaves towards the parents, and how the parents behave towards the child. She can get first-hand information not on one occasion, as when the doctor calls, but on any occasion when she can spend an hour or two in the home.

To prepare the report of the social worker, rough notes are kept, not in any particular order, but recording every detail that she notices, in the home, in the conversation and in the attitude of parents to children. She then makes a chronological summary of that material. This summary is used by the clinician. A complete summary should contain all the relevant material.

The psychologist of a child guidance clinic does not merely fix an intelligence quotient to the child. Intelligence quotients are frequently fallacious and inaccurate, and at best give us only a vague general idea as to the intellectual equipment of the individual concerned. A trained psychologist in a clinic will provide interesting sidelights upon the child in other ways. By observation during the carrying out of standard tests, the psychologist will note the child's attitude towards difficulties, his methods of attack on problems, his reaction to failures, to success, and to assistance. In this way much interesting information can be obtained as to the child's mental attitude towards its environment. Psychologists are able to interpret reports from educational authorities, schools and teachers.

In the case of young children the report of the psychiatrist (apart from the physical examination) is really a small part of the whole case material; frequently the social, psychological and physical reports are sufficient to enable a diagnosis to be made without subjecting the child to any special psychiatric examination. This is a great advantage, as asking the child about his emotional life is frequently harmful, engendering introspection and supplying that limelight the desire for which is itself the basis of so many problems.

The actual amount of psychiatric examination carried out varies directly with the age of the patient. The younger the patient, the less the psychiatry, is a general rule, although on occasion the emotional difficulties of even a small child may be adjusted to a great extent by a short psychiatric talk.

The reports of the different workers having been made out, a case conference is held at which the observers meet and discuss the material they have collected. To this case conference interested parties may be invited—the teacher from the school, the doctor who referred the patient, and so on.

These conferences are useful for individual cases but they are also useful for instructional purposes. Students can attend, hear the methods and learn the interpretation of cases. Cases used for teaching purposes can be easily disguised. At these conferences treatment is decided upon. The psychiatrist, as director of the team, is responsible for the conduct of the case, but he usually delegates certain appropriate lines of treatment to the various members of the team. If psychiatric treatment is necessary, the psychiatrist himself carries it out, the patient visiting the clinic for the purpose. He is also responsible for recommending physical treatment. If the home is difficult, and emotional situations there are prejudicial to the patient, the social worker, on her visits to the home and in conversations with the parents, does her best to attack these, and though it is usually difficult or impossible to alter the emotional attitude of parents towards their children, it is actually found in practice that it can be done.

The psychologist may also take part in the treatment. If a child's problem appears to depend on some special educational difficulty, the psychologist may give the child special tutoring, or help in some disliked subject. A small amount of assistance in one particular subject will often bring the child in line with his fellows in school and give him quite a new start in life.

From time to time during the treatment of the case, further case conferences are held, progress is discussed, difficulties are brought forward and plans for treatment readjusted, if necessary.

It has been found that, although the team method appears to be cumbersome and an unnecessary number of people seem to be working on the same case, it is not so in actual use. There would appear to be a certain disadvantage in having the case handed from one person to another, but this disadvantage is much more theoretical than real, and, in practice, does not constitute a difficulty.

The social workers are chosen for their special adaptability and tact, and they do not create the impression that they are making inquiries. Their visits are simply friendly calls in order to observe what is going on in the home.

Usually the parents of problem children are only too pleased to have a sympathetic ear into which to pour their troubles. If the sympathetic ear happens to be one of the doctor's it is apt to become very irritable, whereas the social worker's is there for that express purpose.

Another aspect of the team method must be mentioned. One of the great advances in child psychology was the development of the experimental method of intelligence testing, coupled with observation of the child in the performance of the intelligence tests.

Many attempts have been made to devise similar series of tests for emotional or temperamental evaluation, but nothing that has so far been evolved is really successful. There have been the physiological methods, the psychogalvanometer, and time reactions. There have been attempts to create artificial situations in which the child was told a story, and one noticed how he reacted towards the situation in the story. There is the standardized psychiatric interview such as is now used more or less by most people dealing with child psychiatry. It is not generally realized that the social worker can be used to produce almost an experimental observational method. That is to say, the social worker in visiting the home can accurately

record the child's reaction towards difficulties in its environment. The properly trained worker can observe so accurately that an experimental situation is to all intents and purposes created, with observation super-added.

The development of the team method makes an important contribution to the study of child behaviour and its associated problems, providing a new and powerful means for investigation and treatment.

Dr. Emanuel Miller: To me the term "difficult child" has grave drawbacks, because all sick children, and indeed children who are not sick but who possess more vitality than is good for their parents, nurses and schoolmasters, may be so described. I shall consider a special class of child, namely the group in which no demonstrable defect of the organs can be found, and in which no metabolic disturbances exist which can be reasonably described as primary. By thus defining my limits I do not wish it to be understood that I am of the opinion that psychological disturbances of an active kind exist in the absence of changes in metabolism. That assertion would be a denial of the well-established relationship between the emotions and the neuro-vegetative processes. My experiences are based almost entirely on the observation of difficult children between the ages of five and sixteen years, made at the child guidance clinic established by the Jewish Health Organization over two years ago. The experiences are drawn from a more or less equal number of Jewish and non-Jewish children, all examined psychiatrically, physically, and by a trained psychologist, and whose family situations have been fully examined sometimes over a space of two years.

A great difficulty of the method that we have adopted—and I choose to deal with difficulties rather than triumphs—has been the relating of the psychological disturbance to the social and familial environment in which it is supposed to have arisen. There is a danger that the established social service of a clinic may lead to the general conclusion that if you can find an environmental error, somehow this can be regarded as the cause of the psychic disturbance. I do believe that there is a correspondence between a behaviour disorder in the child and an error in the home or in the school. Failure of a parent to deal equitably with a youngest child, failure on the part of a schoolmaster to identify a congenital word-blindness, an auditory imperception, or a particularly poor subject may lead to a feeling of shy inferiority or glowering rebellion as compensation. The triple foundation of the modern psychological clinic is admirably suited to detect such situations. But there remains a very large group, in which there is, at most, only an indirect relationship between the family and the social milieu, and the child.

I mean that the family, though socially a unit, is largely a system of discordant persons pulling and dragging in many directions, the result of economic and temperamental forces. Against this is set the child in question, as if he were a tragic actor set against a lurid family and social back-cloth. This is seldom, if ever, a true picture.

The more one looks into such cases the more one is struck by the complicated dynamic complexity of the situation on both sides. A child's rebelliousness or intractable obstinacy is largely of a selective character. A child may steal from one parent and not from another; it may steal particular things, or do so at special times. It may be the angel in the house and the demon in school, or the bane of its mother's life yet the favoured bright boy in the schoolroom. A child may show absolutely no disturbance whatsoever in the most sordid surroundings. A lad was sent to us for observation with regard to the probable dangers of a bad home and a lurid family history of crime, prostitution and insanity. His enuresis was cured, not by altering his relation to a social situation, but by circumcision. Such an example makes it obvious not only that the social situation is much wider than the child, but that the child's disorder may be much deeper than the social situation.

That is to say there are many phenomena that are investigated, vastly interesting as sociological data, but irrelevant. I find it useful to regard the social situation as a stimulus to the child, but whereas the overt behaviour disturbance may be occasioned by that particular social set, what has really happened has been the activation of a situation that has gone before. Efforts to remove the present stimulus will not always touch the true origin of the response. The family must necessarily be regarded as a society held together not only by affective bonds but by bonds of social usage. The first type of bond brings with it the call for love and aid on both sides, that is, on the side of both children and of parents. This bond may be perfectly consistent in character on the part of the parents. Yet each member or perhaps a particular member believes himself to be singled out for harsh treatment or for ostracism. Position in the family frequently has a strange way of determining this feeling. Many a younger child feels that he is not wanted, and I have noted in an appreciable number of cases a "foundling phantasy" shaping itself in the mind. One little girl walked on tip-toe because she believed she was not related to her parents, but had been in fact left by a great lady and had to walk mincingly in order to act the part of one of high birth. Such examples of personal idiosyncrasy of behaviour can be multiplied in illustration of the fact that problems exist which do not present themselves in the sociological picture. I have noted in a dozen or more cases that though children may be bound to parents and brothers by bonds of blood and love, they may be separated by constitutional differences that make them appear, not only to themselves but to others, to belong almost to a different stock. What can make for greater anomalies of behaviour than to feel that you are not a member but a "sport" in a social group? How much more so if this should occur within the narrower confines of the family at a time when the mind is most plastic and therefore takes vivid note of minor shades in the demeanour of others? Social observation, however intense, cannot take full cognizance of nuances of this kind. Where the defects of the environment are manifest on the surface, in gross misunderstanding and mismanagement, in economic stress, and the nutritional defects that follow from this, then the social service is of inestimable value. My colleague (Dr. Noel Burke) and myself can quote cases in which the correction of these evils has led to substantial improvement in the behaviour of a difficult child. But the successes undoubtedly achieved in these cases may veil the deeper significance of symptom and behaviour.

What criterion have we to differentiate between the cases that are, in the main, within the realm of social and educational methods of correction and those that are outside this realm?

Wherever the reactions of the child betray a distinct infantile quality we are probably dealing with a condition which, although evoked by some present circumstances, is in reality the reactivating of some early situation. The mechanism of this reaction is in my opinion the conditioned reflex, the mode of evocation being either the reproduction of a past motor response or the reproduction of an emotional mood. Where the latter is the case we may have disturbances of metabolism, such as vomiting and wasting sometimes quite alarming in degree. I am here reminded of a case of a little girl, pale, wizened and terrified, who had for months past been wetting herself by day and by night. The child had been furtive, and had a dull, stupid, day-dreaming expression. There was no evidence of physical disorder. These matters had been carefully entered into at the London Hospital. She was only slightly retarded in intelligence, but two standards behind in school owing to frequent absence. The family is economically only on the margin of subsistence. The pathos of this family when it visited the clinic was very moving. Although the child's demeanour became less terrified and more friendly after a few visits, little improvement was registered. After an absence of a few weeks she returned to us quite changed. The last baby had then been weaned. An intimate

relationship was broken in the eyes of the young subject. The enuresis ceased, the child's demeanour had changed, her cheeks had the bloom of improved metabolism, she returned to school, and her teacher said that all was well. I must admit some economic improvement in the family and the sympathetic treatment the mother had received at the hand of our social workers. But the fact remains that without any apparent psychiatric help, except perhaps in an obstetric sense, the child's emotional mood had undergone an internal change and with it behaviour and metabolism had returned to the normal.

Another aid to the presence of deeper psychological motivation is the recognition of the presence of magical and symbolic gestures. The recognition of these movements and their differential diagnosis from pure habit-spasms and post-rheumatic movements will prove of great value in the interpretation of a behaviour situation.

A case of head banging in the absence of all organic disease, of walking on tip toe, of reeling, staggering gaits, were all found on the little investigation that our time permitted to be the child's symbolic gesture language for expressing its attitude extra-consciously to a family situation. The physician alone is frequently unable to detect these gestures. They may appear during the periods of psychological testing or during the social worker's local explorations. On this basis alone, if not for the legion of other reasons, the triune organization of child guidance work is in our estimation one of the solid contributions to modern medicine.

Sir Robert Armstrong-Jones (Chairman) said "the difficult child" is perhaps easier to describe than to define, because it seems to me that the same kind of child may be viewed differently according to his social origin and order. The social worker so far as I gathered, is the best diagnostician of the difficult child who fails to adapt himself to a social environment. A child may be "difficult" in a refined social circle who would not be regarded as difficult in a lower stratum of society. For instance, a child who got into tempers and who fought and screamed, would soon be brought to account in a well-regulated home, whereas in the lower scale he would simply be regarded as courageous and spirited. In the lower stratum it is most difficult to get the mother to confess that her child is abnormal, even when this child is weak-minded. The "difficult" child is one who fails to adapt himself to his proper environment. The herd-instinct, for instance, in the normal child leads him to join the Boy Scouts, but too often leads the "difficult" child into mischief and anti-social adventures.

Some of the so-called "difficult" children are obviously mentally defective or weak-minded. They are sleepy, listless, irresponsible and dull. They should, as one speaker said, receive special care and attention, preferably in an institution, or they soon deteriorate. But as a rule, the difficult child is not backward or mentally defective, but is quick and responsive. He is often precocious, has a "good shop window," and puts the right foot forward, but he has an impish malignity. He may throw the cat on the fire or out of the window, may pinch other children and say somebody else was the culprit, may lie and steal, and is never ashamed of his own perversity. These are the little "freaks" and "oddities," who come under the designation of "moral imbeciles." The two extremes are easily recognizable. But the large intermediate group is, as Dr. Cameron said, more difficult to diagnose, and still more difficult to treat. The children in this group are often the subjects of habit-spasms or tics; they have facial twitchings, are often restless by day and sleepless by night, or wake up with night terrors, or wet the bed; they may run away from home and play truant, and they are irritable and self-willed. These children should be kept to a quiet daily routine, and their diet should without doubt be that which Dr. Cameron has suggested. These highly-strung "nervous" children have an infinity of symptoms; they require special care to keep them "on the rails." Mentally they are unstable, and lacking in self-control and self-direction, and it is difficult to fix their attention.

If these difficult children are neglected, they may become law-breakers and a not inconsiderable number of them figure in the juvenile courts. They may become alcoholics or drug addicts, and they often swell the ranks of the unemployable. Some drift into certification, and a few come under good training and useful teaching, and so make useful citizens.

I am a firm believer in the influence of environment. Given a suitable environment of sympathy, interest and work, much can be done, at school and elsewhere, to make the difficult child much less so.

Dr. T. R. Hill: I wish to speak—with a reference to their treatment—of two organic pathological conditions of the nervous system which produce in children a disorder of behaviour, with no gross or commensurate abnormality or diminution of intelligence, the disorder of behaviour being such as to make them typically "difficult" children. These two conditions are chronic epidemic encephalitis and non-encephalitic dyspituitarism. They are both characterized by the exhibition of behaviour which is crudely instinctive in type. In the normal child crude instinctive responses are readily evoked by innumerable appropriate stimuli. Nothing is more familiar than the outbursts of anger, fear, acquisitiveness and gluttony, etc., of childhood. These outbursts occur in the cases of behaviour disorder following epidemic encephalitis but in a highly exaggerated and uncontrollable form so that the child becomes a slave to them, exhibits them constantly, and is at the mercy of the various situations that evoke them. It is the exaggeration of these crude instinctive forms of behaviour, familiar in a minor degree in normal children, that constitutes the typical case of encephalitic behaviour disorder.

I have elsewhere described the evidence that suggests that the optic thalamus, particularly the essential organ of the thalamus, is an area of the brain associated with crude instinctive behaviour and emotion. I have also attempted to show that the alkaloid bulbocapnine is a powerful cerebral depressant with its main action on this area of the brain, which means psychologically that its chief effect should be a specific depression of instinctive tendencies and crude emotion. There is much experimental evidence in favour of this suggestion, some of which will be revealed in describing the action of the drug in cases of encephalitic behaviour disorder.

The drug exerts for several hours after administration a specific effect upon the aberrant behaviour with very slight evidence of any other action at all. In fact in many cases it exerts absolutely no effect at all except a markedly specific one upon the abnormalities of behaviour.

I have employed the drug with a large measure of success in about thirty cases.

The extremely specific action of the drug is shown by the fact that the greater the outburst of crude emotion, the greater is its effect. Severe cases of encephalitic behaviour disorder often exhibit great displays of anger and combativeness which may last for hours. A hypodermic injection of bulbocapnine given by force has an instant effect in subduing these, the patients becoming quiet and normal within ten minutes. No other drug that I have tried has produced anything like this effect.

Briefly some of the other characteristics of this alkaloid are: (1) It sometimes produces, immediately after administration, a short period of light somnolence. There is much evidence to suggest that this is a state of natural sleep, and that it is not to be compared with the somnolence produced by a drug obeying the law of dissolution, such as a general anæsthetic; (2) it produces no toxic or cumulative effects; (3) tolerance is very slowly if at all established, and (4) the patients relapse after omission of the drug.

A form of behaviour disorder with clinical characteristics identical with the familiar encephalitic form, occurs not infrequently in non-encephalitic dyspituitarism. Dr. Worster-Drought has described to me a number of such cases that he has met

with and he has found that behaviour disorder may occur in (i) those patients showing a tendency to gigantism, etc., from hyperfunction of the anterior lobe; (ii) those showing decreased posterior lobe function with dystrophia adiposo-genitalis, and (iii) in mixed types. Berman has mentioned similar cases. I have been able to observe, over a period of two years, one patient suffering from this condition—a boy, now aged 14. He displays typical moderate dystrophia adiposo-genitalis and possesses good intelligence. For three or four years he has been constantly badly behaved, being restless, impulsive, untruthful and addicted to frequent thieving. No punishment, admonition, or pleading, etc., from his parents, who seemed very sensible, had any effect. On September 29, 1929, 0·1 grm. bulbocapnine was given to him by mouth, and this has been continued every morning since. A marked improvement in his behaviour was evident at once. After one week his behaviour was said to be normal. This improvement has continued without relapse to the present day.

The great interest of these cases lies in the suggestive link that they form between the mental and physical aspects of emotion. I think that the physical rôle of thalamic function in the genesis of emotion and instinctive behaviour, about which there is some conclusive evidence, is a neuro-psychological subject which has been somewhat neglected and which will repay further study.

Dr. D. W. Winnicott, while acknowledging the existence of the physical changes described by Dr. Cameron, said that it was necessary to recognize the non-physical basis of emotional disorders. He thought that there was a field for child guidance clinics, but considered that work which ignored the fact that symptoms usually represented an attempt at spontaneous cure for a disease due to conflict in the unconscious, must be very limited.

Miss Mary Chadwick said that though diagnosis was the first important point, the great question was: What was to be done afterwards? Would these children be treated by the social worker's talking to the parents? It had been said that the difficulties which arose often represented repressed tendencies on the part of the parents; but a diagnosis would not cure anybody, and even explaining repressed tendencies, whether of adults or children, would not help very much. It was necessary to go further and do something. She would like to know what the Child Guidance Council did by way of treatment. Of what did the psychiatric "talk" consist? Was it merely advice? She did not know that anybody thought of directly questioning a child about his emotions; if they did so she did not think there could be much response, because the child could not state in words what he felt. By various methods of treatment and observation one could realize how the child expressed his emotions and his phantasies, and something of this kind must be done before one could expect to get the child free. In some of the German clinics they made a point of treating the parents as well as the children, should a neurosis in one or both parents seem to have been the main predisposing cause of the nervous trouble in the child.

In any case, the psycho-analytic clinics in Germany, Vienna and Paris considered it necessary to deal with the problem of the difficult child by definite psychological treatment, administered by properly trained analysts.

Dr. Noel H. M. Burke said that out of fifty cases on his records, thirty provided facts sufficiently definite for consideration. The home was at fault in twenty-three out of the thirty, the mind of the child was wrong in twenty-four, the school in seven, the child's bodily health in fourteen. He tried to give a valuation to these after the manner of Dr. Cyril Burt. Home difficulties came first with 29 points, mind 15½, health 8¼, school 4½. In the home there was dis-harmony

and defective handling of the child; in one case there was criminality in the father, who was in prison. Occasionally the fault was only a small thing, such as defective sleeping accommodation. Among the cases in which the school was to blame, in some the work was too hard, in some too easy. Sometimes the work was not adjusted to the particular case, some special work was required, or attention to the tuition in a special subject. In some cases the discipline was too strict for the child.

Every child was completely examined physically. In one case the trouble disappeared after the removal of tonsils and adenoids. One had cyclical vomiting, one had had tuberculous joints for years. Two were heart cases, and in two the trouble was largely due to visual defects.

There was subnormal intelligence in nine cases, definite dullness in five, a state of almost feeble-mindedness in two. Two were definitely defective. In one girl the intelligence quotient was 136; her intelligence and her consciousness of it were such that she could never fit in with the surroundings in which she had been born. All had various anxieties, fears, or definite neuroses.

As Dr. Moodie had said, parents did not like the accusation of inadequacy, and there, the speaker thought, was the greatest difficulty; it was the home more than anything else which required to be readjusted. In two cases in the series under review nothing could be done, because the parents were inaccessible to either advice or suggestion. There was partial amenability to adjustment in twenty-four instances, and good in four, which meant that there was good coöperation on the part of all concerned.

As to general results, there was successful adjustment in six cases, fairly good in nineteen, slight in three, complete failure in two.

What were the adjusting methods? One patient was sent to Winchmore Hill Hospital as a probable case of post-encephalitic-behaviour disorder. It was there decided that she was epileptic, and she had now gone to an appropriate colony. Some cases needed a residential school, where they lived a well-ordered life, the discipline being guided by understanding and reason and where they obtained removal from impossible homes. Children who came to a child guidance clinic could not be sent to a residential school except with the help of the court, and three were so sent to Home Office special schools. In four cases scout and guide training was the essential thing. In one case a Jewish boy was put into touch with the proper quarter so that he could attend the customary classes in Hebrew, his family being careless of such duties. He was now happy because he was doing what social pressure required of him.

Dr. J. R. Rees said that the point of view taken by Miss Chadwick was the Freudian approach to this subject and the antithesis of Dr. Cameron's approach. Very few people, so far as he knew, were doing serious child-analysis in this country, and the same was true of America. Even in Vienna there seemed to be a tendency to give up the method. The experience of those who had worked in the Children's Department at the Tavistock Square Clinic for the past nine years was that a set analysis was not needed. The really important point in treatment was that the doctors who were dealing with difficult children must have the analytical point of view.

A good deal of what had been said about environmental treatment had seemed to him (the speaker) to be vague. Such methods would necessarily be vague unless those who prescribed them had enough insight into the psychological difficulties of the child to prescribe wisely for him and also to educate the parents and teachers concerned. It was of no use to put a child into a foster-home or institution, unless such an institution suited the individual case, so that the staff were able to deal intelligently with the various psychological difficulties that had manifested themselves.

Dr. **Margaret Lowenfeld** said it was often found that the child who had been removed from his home to more favourable surroundings, greatly improved, but after he had returned home, the same type of difficulty was renewed, the same reaction was observed. It was hard to find a method of approach to this subject which was not strictly analytical but yet not purely environmental. The key was an understanding of the child's relationship to the world and his comprehension of it. She thought much more would come to be done by adopting means whereby the child could express his own phantasies. Then these could be, little by little, interpreted by himself. In this way he would learn to stand on his own feet, and would come to understand the reasons for his own behaviour.

The emotional difficulties of the child were often induced by, or associated with, biochemical or physiological disturbances, and particularly with disturbances of posture and general behaviour. There were cases which showed a definite correlation (i.e., such things as the acid-alkali balance) between the physical and the emotional state of the child. Thus, one could approach the problem from two sides: either by altering the physiological side and thereby bringing about an emotional change, or vice versa.